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SOME CHARACTERISTICS OF THE MEDICINE IN SHAKESPEARE

By Arthur W. Meyer,

Instructor in Anatomy at The Johns Hopkins University.

But why should I dead Shakespeare's praise recite?
Some second Shakespeare must of Shakespeare write.
—Leonard Digges.

If it be a rule that no one should write about Shakespeare without a license I stand convicted. I have no license and cherish no hope for any. Neither am I a "thorough antiquarian" or "heaven-born critic" as Leslie Stephen prefers. Yet, since the master whom "I serve quickens what's dead," I trust that this delineation, the product of *horæ subsecivæ*, may not prove "as tedious as a twice-told tale vexing the ear of a drowsy man."

To those familiar with the literature on the medicine of Shakespeare, many reasons for further study of this too oft rediscovered subject will come to mind. It is not my purpose, however, to "anatomize" specific medical references or to pass judgment upon the medical knowledge of Shakespeare. Far be it from me. Such a judgment cannot be based upon the plays alone. Shakespeare's knowledge of medicine and his attitude toward physicians may be reflected in his plays, but this seems to be merely incidental. Obviously, if the characters in Shakespeare express medical facts, Shakespeare himself must have possessed a knowledge of these facts. However, it is the world's life rather than his own that the great dramatist reveals to us in his dramas.

The medical writers of the sixteenth century interested themselves more with the medicine of Hippocrates, Galen, and Rhazes than with that of their own day. Hence it is difficult to form a good conception of the medicine of Shakespeare's time. The death of Vesalius, a few months after the birth of Shakespeare, is perhaps one of the greatest of landmarks. Vesalius's enforced expiatory pilgrimage to the Holy Land, in order to escape sentence by the Spanish Inquisition, vividly recalls the temper of the times. Fancy and imagination were unbridled, suffer who might through the accusations of excited and misguided individuals! Galenism was still supreme. Physicians clung to Galen and accused of heresy all who did not accept his teaching. Hospitals were still in the hands of the priesthood but medicine and surgery had passed from their domination. Yet the activity of the priesthood continued. Almost a century later Gideon Harvey exclaimed, "In short *libera nos* from those who practice medicine in *Nomine Domini*." The Royal College of Physicians, of London, was forty-six years old, and a union of Barber Surgeons and Guild Surgeons known as the Company of Barbers and Surgeons had existed since 1540. Physicians held secreta against the rule; surgeons as a rule. The former wrote in Latin, the latter, though learned, in the vernacular and were ostracised and roundly berated for it. Neither "learned nor unlearned" surgeons had statutory powers. They could not give internal remedies, and their bitter disputes with physicians were to last for centuries. They were slowly freeing themselves, however, from the barbers and

were demanding recognition from the physicians who were loath to grant it. The dictum of Galen that a physician need have no knowledge of surgery still remained the gospel of physicians and the bane of surgeons. However, heroic voices were being raised against the abuses in medicine and physicians no longer deemed it a disgrace to visit their patients. The first herbals had just appeared, yet grocers and apothecaries were still in one company. The latter charged exorbitant fees, prescribed on the reported diagnosis of physicians, and even changed the prescriptions of physicians at will. The value of pathological anatomy had been pointed out, but gynecology, and especially obstetrics, had received but little attention. Yet these were days of universal awakening. Great seats of learning had arisen. Naples, Bologna, Padua, Ferrara, Montpelier, and Paris were famous and destined to become historic. Anatomy had, indeed, made great progress. Vesalius, Fallopius, Eustachius, Sylvius, Aurantius, Bauhin, Spigelius, Botal, and Glisson, were its greatest devotees; and da Vinci, Calcar, Dürer, Michael Angelo, Titian, and Raphael, its artist patrons. Dissections of the human body to which surgeons were summoned by a beadle were made annually in London. These dissections taught physicians to believe their own eyes and to cease apologizing for the inaccuracies in Galen with the plea that human beings were formed differently in Galen's day. Back to the Bible for the theologians became back to the cadaver for the anatomists! The great pestilences which periodically swept over England and over all Europe left the country prostrate. Among these whooping-cough and pleurisy had made their advent. It was customary to look to God, to the stars, and to the devil for the causes, but the pall of superstition was lifting. The world was astir. These were, in short, "the spacious times of great Elizabeth."

To read Shakespeare with a purpose is no easy task. Felicity of expression, interest of plot, depth of pathos, and beauty of character hold one in a magic spell, entirely oblivious of one's quest. Whole pages, scenes, and, perchance, acts must be re-read with the purpose freshly in mind. Consequently any list of medical references obtained by a single reading must be incomplete. However, such a list has been supplemented by consultation of different editions and by comparison with the compilations of various authors. An examination of these references in the light of the medicine of the sixteenth century, of the England of Shakespeare and *of the genius of Shakespeare,* ought to reveal to us the leading characteristics of the medicine of Shakespeare. To examine them, as is so often done, in the light of the present day, is a serious error. For, as Leslie Stephen has well said, "It is, of course, an anachronism to transplant our problems to those days." That this anachronism has frequently been committed even a cursory examination of the literature will show. Things have repeatedly been read into the plays of Shakespeare rather than out of them. Many amusing examples might be given illustrating how "hateful error" has shown "to the apt thoughts of men the things that are not," or that there is no "damned error, but some sober brow

Will bless it, and approve it with a text."

The number of medical references found will vary with the edition used and with the *medical* and *historical perspective of the reader.* A liberal interpretation will naturally include many things which are merely matters of knowledge common to all men. Such, for example, are the following:

He that sleeps feels not the toothache.
—*Cymbeline*, V, 4.

We do lance diseases in our bodies.
—*Antony and Cleopatra*, V, 1.

'Tis dangerous to take a cold.
—*Henry IV*, Pt. I, II, 2.

The more one sickens the worse at ease he is.
—*As You Like It*, III, 2.

Many will swoon when they do look on blood.
—*As You Like It*, IV, 3.

. . . . . a gaping wound
Issuing life blood.
—*A Merchant of Venice*, III, 2.

What wound did ever heal but by degrees?
—*Othello*, II, 3.

That rubbing the poor itch . . . . .
Make yourselves scabs.
—*Coriolanus*, I, 1.

To this class of references belong also the change of voice at puberty, the mere mention of fever, nausea, and God's tokens, the loss of appetite in disease, the obstruction of blood by tight garters, vomiting after surfeiting on sweets, and many medical references which were a part of the superstition of the time. Indeed, the fact that medicine and physicians were surrounded by an atmosphere of superstition often makes it difficult to discriminate between the many vulgar beliefs of that day and medical allusions. The unwary student may thus regard as idle superstition lines pregnant with medical lore. The language, too, in which these medical facts are expressed will depend to some extent upon the edition used, and the meaning of some of them remains obscure and disputed even after the most careful comparison and diligent inquiry. Among these may be mentioned the expressions "hollow bones," "sand-blind," "hebenon," "goodyear and eyesel," for which various explanations have been suggested. In other cases the language is clear but the meaning is obscure. This is true of Portia's method of suicide, of the nature of Cardinal Beaufort's delirium, and in a measure of Ferdinand's avowal,

"I warrant you, sir,
The white cold virgin snow upon my heart
Abates the ardor of my liver."
—*Tempest*, IV, 1.

There remains the important and vexed question of authorship. As a basis for these remarks only those plays or parts of a play which are considered truly Shakespearean have been used. However, the final estimate of the medicine of Shakespeare would not be materially affected by ignoring the

question of authenticity or by adopting either a liberal or a narrow interpretation regarding what shall and what shall not be considered a medical allusion.

The number of medical references in the different Shakespearean plays varies considerably. As might be expected comedies as a rule contain fewer than the tragedies and historical plays. In the historical plays, and especially in the tragedies, pestilences and their supposedly mysterious and evil origin, poisons with their strange and sinister powers, and death with its consequent political intrigues and conflicts, its trials and pathos, offer a necessary material. The poems and sonnets contain at most a few dozen references, and the greater number of these are found in the Rape of Lucrece. They embody nothing especially characteristic save that the medicine of some of them, like the surgery in Titus Andronicus, is quite impossible. If we except Henry IV and VI, the later plays contain more medical expressions than the earli nes. Yet it seems impossible to demonstrate—what must have taken place—a definite growth in Shakespeare's medical horizon. Henry VI, which belongs in the first years of Shakespeare's literary activity, contains more numerous medical references than any other play. This, however, is largely accounted for by its being composed of three parts, thus making a much longer play. The same is true of Henry IV. However, the important thing is not the actual number of references in any one play, but rather the total number which are found in Shakespeare's earlier, as compared with his later, works. Among other plays containing many medical references are King John, Coriolanus, Othello, Troilus and Cressida, the Winter's Tale, and Hamlet. Plays in which a physician enters contain no more medical references. Strange as it may seem at first sight, the physicians are minor characters who contribute little or nothing to the fund of medical knowledge. The words which they utter could usually be spoken by anyone in their stead. Their presence is, as a rule, demanded by the dramatic purposes of the plays. Cornelius, in Cymbeline, for example, forms part of the dramatic machinery used to protect Imogen from a cruel death, thus affording an opportunity to develop and complete the plot.

A great many of these medical facts are expressed in the form of metaphor and simile. Although the use of the simile is especially frequent but few of these figures of speech are inaptly used. Many are sustained, consistent, and effective. Hotspur, in replying to Glendower's assertion that the earth shook when he was born, tells him that

> "Diseased nature oftimes breaks forth
> In strange eruptions; oft the teeming earth
> Is with a kind of colic pinch'd and vex'd
> By the imprisoning of unruly wind
> Within her womb; which, for enlargement striving
> Shakes the old beldam earth and topples down
> Steeples and moss-grown towers. At your birth
> Our grandam earth, having this distemperature,
> In passion shook."
>
> —*Henry IV*, Pt. I, III, I.

In the light of the gynecology of Shakespeare's day this figure is entirely consistent. One of the "Observations" of Dr. John Hall might also be quoted in corroboration of this, did the quaint phraseology permit.[1] "Wind in the womb" was a clinical entity in those days. The most sustained simile is that on the Belly and its Members in Coriolanus, which consists of thirty-two lines. Its inconsistency is explained by Menenius himself in pointing out that "The Senators of Rome are this good belly" and not the body politic, because . . . . "No public benefit which you" [the individuals composing the state] "receive

> But it proceeds or comes from them to you
> And no way from yourselves."

He concludes with the taunt

> "What do you think,
> You the great toe of this assembly?"
>
> —*Coriolanus*, I, 1.

The use of elaborate figures of speech might seem to presuppose a thorough knowledge of medicine. However, we must remember that the language of Shakespeare abounds in rich imagery. What remained bald medical facts in the hands of his literary contemporaries, Peele, Marlowe, and Greene; yes, or even rare Ben Johnson, was dressed in incomparable English by him. This is trite, I know, yet a quotation from Ben Johnson's Magnetic Lady (II, 1) will emphasize it:

> "He would keep you . . . . . not alone without a husband
> But in a sickness; ay, and the green sickness,
> The maiden's malady; which is a sickness,—
> A kind of disease . . . . .
> Give her vent
> If she do swell, a gimlet must be had;
> It is tympanites she is troubled with.
> There are three kinds: the first is anasarca,
> Under the flesh a tumor: that's not hers.
> The second is ascites, or aquosus,
> A watery humor; that is not hers neither;
> But tympanites, which we call a drum,
> A wind bombs in her belly, must be unbraced,
> And with a faucet or peg, let out
> And she'll do well: get her a husband."

These lines contain much medical lore but little poetry. How Shakespeare's genius would have transformed them! His was the magician's wand and he while

> "A thousand poets pried at life
> Alone rose to be Shakespeare."

If we compare the medical facts found in Coriolanus, Antony and Cleopatra, Julius Cæsar, Cymbeline, Lear, Macbeth, King John, and Henry VIII, it is impossible to distinguish one from the other. Coriolanus lived 430 B. C., Antony and Cleopatra and Julius Cæsar in 69 B. C.; Cymbeline and Lear in legendary England; Macbeth prior to 1056 A. D.; King John from 1199-1216 A. D., and Henry VIII from 1509-47. Consequently from Coriolanus to Henry VIII we have a period of 1977 years. Within this great period of time medicine, of course, went through various phases of develop-

[1] Cf. Aetius Chpt. XXXI. Diversum affectionum ob quas mulieres non concipiunt, curatio; also, Soranus, Chpt. LVI and LXXVIII.

ment. None of these phases is represented in the medical references in Shakespeare save as preserved in the superstitions and the medical lore of the common people and of physicians. It has been pointed out that the idea of the circulation of the blood given in Love's Labor's Lost is not as recent as that given in Coriolanus, and this fact has been used to show that Shakespeare must have kept abreast of the progress of medicine. Unfortunately for those who advance this argument, Menenius's words on the Belly and its Members have been traced to various non-medical sources which were undoubtedly accessible to Shakespeare. No attempt seems to have been made to harmonize the medicine with the time and scene of a play. The speech in which Timon enumerates so well many of the symptoms of secondary lues is a good illustration of this. Although Timon, the misanthrope, lived four centuries before the Christian era, yet he possesses the medical knowledge of the sixteenth century. A parallel to this is found in Hamlet, the thoughts and language of which are those of Christian England of the sixteenth century, while the scenes and characters belong to heathen Denmark of the twelfth century. Wherever, as in the case of the description of the apothecary's shop in Romeo and Juliet, there appears to be an adaptation, we find it to be mere coincidence and due to the sources from which the plays were taken. What is true of the language of Shakespeare is largely true of the medicine of Shakespeare. Both represent the England of Shakespeare.

Among the characters which possess a knowledge of medicine we find every walk of life represented. Doll, Mrs. Quickly, Pandolph, Falstaff, Boult, Speed, Biron, Leontes, Marcius, Ulysses, Iago, Friar Laurence, Holofernes, Warwick, Troilus, Titania, Brutus, Casca, Portia, Cleopatra, Cæsar, King Richard, Cerimon, Helena, Cornelius,—but where is the end? A motley procession. Libertine, wise-woman, servant, artisan, friar, schoolmaster, courtier, royalty, medical dilettant, and physicians,—all speak words of wisdom (?) on the great questions of health, of diseases and their cures, and of life and death. Those lowest in rank seem to have the greatest knowledge. Perhaps because theirs was the greatest need. No one takes more delight in airing his medical knowledge than the inimitable Falstaff. He is the man of the world and his is the experience of the world. It is he who knows about the treatment of *morbus gallicus* and he who expresses the most advanced ideas regarding contagion.

The medical knowledge of Shakespeare is held in common by all classes. There is no essential difference between what courtiers, kings, and queens know, and the medical knowledge of Doll, Mrs. Quickly, and Falstaff. The following quotations will serve to illustrate this point. Ulysses, the crafty politician and general, says:

> " . . . . . but when the planets
> In evil mixture to disorder wander,
> What plagues and what portents."
>
> —*Troilus and Cressida*, I, 3.

> " Be as a planetary plague, when Jove
> Will o'er some high-viced city hang his poison
> In the sick air: "
>
> —*Timon of Athens*, IV, 3.

rages Timon, a noble, in his pride.

When Hamlet's deportation to England has been decided upon the King says to his courtier Rosencrantz:

> " This sudden sending him away must seem
> Deliberate pause: diseases desperate grown,
> By desperate appliance are relieved,
> Or not at all."
>
> —*Hamlet*, IV, 3.

This opinion of cure by opposites is expressed also by Benvolio when he counsels Romeo for his love sickness, thus:

> " Tut, man, one fire burns out another's burning.
> One pain is lessen'd by another's anguish;
> Turn giddy, and be holp by backward turning;
> One desperate grief cures with another's languish:
> Take thou some new infection to the eye,
> And the rank poison of the old will die."
>
> —*Romeo and Juliet*, I, 2.

In his malediction on Prospero, the monster Caliban prays that

> " All the infections that the sun sucks up
> From bogs, fens, flats, on Prosper fall, and make him
> By inch-meal a disease! "
>
> —*Tempest*, II, 2.

Similarly, Titania laments:

> " Therefore the winds, piping to us in vain,
> As in revenge, have suck'd up from the sea
> Contagious fogs; which falling in the land
> Have every pelting river made so proud,
> That they have overborne their continents: . . . .
> Therefore the moon, the governess of floods,
> Pale in her anger, washes all the air,
> That rheumatic diseases do abound."
>
> —*Midsummer-Night's Dream*, II, 1.

Consumption is referred to by Falstaff, and Timon in the following words:

> " Consumption catch thee."
>
> —*Timon of Athens*, IV, 3.

> " Consumption of the purse . . . . . is incurable."
>
> —*Henry IV*, Pt. II, I, 2.

> " Consumptions sow
> In hollow bones of man."
>
> —*Timon of Athens*, IV, 3.

Rheum is spoken of by Iago, Polixenes, the French King, Pandarus, Aumerle, Anfidius, and others. Mandragora is mentioned by Iago and Cleopatra; henbane by Banquo and the Ghost; the pox by Iago, Speed, Katharine, and many others. It is needless to quote further or to multiply instances in which persons of widely different rank express similar medical knowledge. It is obvious that it would be impossible to learn the rank of the character from a given medical reference. Indeed it would be impossible to recognize the physicians themselves from the facts which they express. The three characters which show the greatest medical knowledge in a single utterance are not physicians, but laymen. Thersites,

the deformed Grecian slave, who plays the rôle of a fool, curses the Grecian commander, Patroclus, thus:

"..... Now, the rotten diseases of the south, the guts-griping, ruptures, catarrhs, loads o' gravel i' the back, lethargies, cold palsies, raw eyes, dirt-rotten livers, wheezing lungs, bladders full of imposthume, sciaticas, limekilns i' the palm, incurable bone-ache, and the rivelled fee-simple of the tetter, take and take again such preposterous discoveries!"

—*Troilus and Cressida*, V. 1.

Biondello, a servant of Lucentio, knows almost as much about veterinary medicine as Thersites about the diseases of the South. Ichabod Crane and his broken-down plow-horse form scarcely a rival to Petruchio and

"his horse hipped with an old mothy saddle and stirrups of no kindred; besides, possessed with glanders and like to mourn in the chine; troubled with the lampass, infected with the fashions, full of wind galls, sped with spavin, rayed with the yellows, past cure of the fives, stark spoiled with the staggers, begnawn with bots, swayed in the back and shoulder-shotten; near-legged before and with half checked bit and a head stall of sheeps' leather which, being restrained to keep him from stumbling, hath been often burst and now repaired with knots; one girth six times pieced and a woman's crupper of velure which hath two letters for her name fairly set down in studs, and here and there pieced with pack thread."

—*Taming of the Shrew*, III, 2.

It is not necessary to say that a horse with all these diseases would not have been ridable! The haughty, immoderate, and reviling Timon, having lost all faith in his fellowmen, exclaims:

"Consumptions sow
In hollow bones of man; strike their sharp shins,
And mar men's spurring. Crack the lawyer's voice
That he may never more false title plead,
Nor sound his quillets shrilly; hoar the flamen,
That scolds against the quality of flesh
And not believes himself; down with the nose,
Down with it flat; take the bridge quite away
Of him that, his particular to foresee,
Smells from the general weal; make curl'd-plate ruffians bald;
And let the unscarred braggarts of the war
Derive some pain from you."

—*Timon of Athens*, IV, 3.

Some of the characters express what their prototypes said, or what is found in the sources from which the plays were taken. This is true of the cure wrought by Helena; of the cure of the King's evil in Macbeth; of the notion that a drug could be set like an alarm clock and could cease to act for "two and forty hours." This was taken from the Italian of Bandello, translated by Arthur Brooke.

"No pulse shall goe, no hart once beate within thy hollow breast,
But thou shalt lye as she that dyeth in a traunce."

—*Matteo Bandello—Romeus and Iuliet*, l. 2156.

The drugs spoken of in the plays of Shakespeare are chiefly such as were in daily use among the common people. Many of those that were not in use by them as home remedies were like familiar objects to them. Foxglove or digitalis, deadly nightshade or belladonna, hemlock or conium, henbane or hyoscyamus, and mandrake or mandragora all grew by the roadside. Some of these, as the "whoreson mandrake" were familiar largely because of the dread superstitions associated with them. Juliet refers to one of these in her fears of "So early waking" after taking the "distilled liquor" prepared for her by Friar Laurence,

"With ..... shrieks like mandrake torn out of the earth
That living mortals hearing them run mad."

—*Romeo and Juliet*, IV, 3.

The method by which the roots of this plant were obtained is shown in reprints of an illuminated manuscript. The figure shows two plants, to the leafy top of which a cord is fastened, the other end being tied to a dog's neck. In its struggles to free itself the dog was supposed to uproot the plant. These roots which were thought to have the human form are, strangely enough, represented by *male* and *female* figures. The poisonous character of monkshood or aconite were also known for centuries, although the therapeutic properties were not discovered until 1762. If we consider "cursed hebenon" or "insane root" to refer to the yew, then this too belongs among familiar plants. Nor is it at all unlikely that the virtues of "parmaceti for an inward bruise" or those of mercury at a time when the best surgeons still wrote "in laudem mercuriæ," were known to the laity. Falstaff surprises us, perhaps, by his enumeration of aphrodisiacs and by his entire familiarity with the customary treatment of lues. But why should not he know of both? It is he who knows all sorts and conditions of men and women. He has "hung loose" on the world, knows it at first hand, says what he thinks, and "blurts it out like a schoolboy." Moreover, if we compare Falstaff's knowledge of drugs with that of John Heywood's *Poticary* we shall be able to estimate it better. This *Poticary*, we recall, as one of the characters in "A newe and a very mery enterlude," a "playe called the Foure PP." When the Pedler, another of the Foure PP., asks:

"Then is that medycyn a souerayn thynge
To preserue a man from hangynge,"

the Poticary answers thus:

"If ye wyll taste but thys crome that ye se,
If euer ye be hanged, neuer truste me!
Here haue I diapompholicus,—
A speciall oyntement, as doctours discuse,—
For a fistela or a canker
Thys oyntement is euen shot-anker,
For thys medecyn helpeth one and other,
Or bryngeth them in case that they nede no other.
Here is syraups de Byzansis,—
A lytell thynge is i-nough of this,
For euen the weyght of one scryppul
Shall make you strong as a cryppul,
Here be others, as diosfiolios,
Diagalanga, and sticados,
Blanka manna, diospoliticon,
Mercury sublyme, and metridaticon,
Pellitory, and arsefetita,
Cassy, and colloquintita.
These be the thynges that breke all stryfe
Betwene mannes syckness and his lyfe;
From all payne these shall you deleuer,

And set you euen at reste for-euer.

* * * * * * * * * *

Not one thynge here particularly
But worketh uniuersally,
For it doth me as muche good when I sell it
As all the byers that taste it or smell it."

—*The Foure PP—John Heywood.*

Many of the remedies, such as cobweb, flax and eggs and keys for bleeding, were time-honored. This is true also of salve and heat for burns, plantain for broken shins, stewed prunes, a dry diet and tubs for those who had that in which, according to Lysimachus,

"A man may deal withal, and defy a surgeon."

—*Pericles*, IV, 6.

What has been said regarding the drugs and remedies applies likewise to most of the diseases, diseased conditions, and symptoms spoken of. To give a complete list would be tiresome. Among the commonest diseases we find rheums, agues, plagues, venereal diseases, leprosy, green-sickness, colic, spasms, "pin and web" or cataract, and "measles." The list of diseased states contains kibes or chilblains, boils, scars, carbuncles, fistula, abscess, gangrene, harelip, birth marks, fracture, dropsy, and others. Most of these, as well as such symptoms as the loss of appetite, and altered taste in disease; vomiting after surfeiting on sweets; obstruction of the blood by tight gartering; change of voice at puberty, were all known to "the general." Certainly no one having once seen the red cross with its accompanying legend "God have mercy on us" over the doorways of sealed houses containing the hopelessly sick and deserted patient, could ever forget the meaning of plague spots or "God's tokens" of death. The use of sputum, facies, pulse, and urine in the diagnosis of disease were daily occurrences in the life of physicians and of scores of those who were not physicians. Consequently we find various characters in the dramas speaking of their use.

The technical expressions are few, come from the lips of lay characters, and have in some cases been traced to non-medical sources which must have been familiar to Shakespeare. This is probably true of the expression *hysteria passio*. Other terms not so familiar to the tongues of men are: tent, of the surgeon; tremor cordis; pia-mater; serpigo; carbuncle; Carduus Benedictus; organ; function; cicatrix; abscess, and mandragora. It is very peculiar that when Shakespeare refers to the popular superstitions connected with the last-named plant he calls it mandrake, but when its therapeutic uses are spoken of he uses the term mandragora instead. Besides these technical expressions the truly wonderful delineations of madness, apoplexy, old age, and death have frequently been mentioned as showing that Shakespeare's medical knowledge as displayed in his plays was not only abreast, but in advance, of the state of the medicine of his day. The descriptions of madness found in the characterizations of Lear, Hamlet, Ophelia, and Lady Macbeth are familiar to everyone. It has been claimed that in his treatment of insanity by means of music, rest, and gentle conduct toward the patient, Shakespeare was several hundred years ahead of the physicians of his time. Be that as it may, for the present it is well to remember that many of the beggars who roamed the streets were madmen, and that the treatment of the insane, cruel beyond all description, might well awaken Shakespeare's compassion. They were bound, flogged, and cast into dungeons. Here they were chained, starved, and often made the objects of amusement for the nobility. Pitied by few, but most of all by Shakespeare in the touching words of Romeo:

"Not mad, but bound more than a madman is;
Shut up in prison, kept without my food,
Whipped and tormented, and—God—den, good fellow."

—*Romeo and Juliet*, I, 2.

Oh, the pathos of that ellipsis! As far as the delineations of insanity are concerned we must remember that it was customary to introduce mad-scenes into plays. Such are to be found in those of Marlowe, Green, and Peele. Not as good mad-scenes as those of Shakespeare, to be sure. Far from it. But they were not Shakespeares. Laehr in his "Darstellung krankhafter Geisteszustände in Shakespeare's Dramen" says that the conception of insanity and its origin in mental and bodily states was given Shakespeare, but that he was a far better observer and knew better how to apply his knowledge of disease than did his literary contemporaries. Laehr concludes as follows: "Uberall ergeibt sich also bei genauer Nachforschung, wie sehr sich Shakespeare in den wissenschaftlichen Anschauungen seiner Zeit bewegte, und wie gerade er das für seine Zwecke passende heraus zu greifen und zu beleben wusste."

We know that the company of players of which Shakespeare was a member had to leave London on several occasions because of the presence of the plague. Hence it is not surprising that it is often referred to. A few excerpts from Pepys' Diary may serve to recall its dreadful visitations. Although Pepys wrote of the great plague of 1663-5, the pictures of its earlier ravages are similar. On June 29, 1665, Pepys wrote:

"To White Hall, where the Court full of waggons and people ready to go out of town. This end of the town every day grows very bad of the plague."

July 12, 1665:

"A solemn fast day for the plague growing upon us."

July 30, 1665:

"It was a sad noise to hear our bell to toll and ring so often to-day, either for death or burials."

August 10, 1665:

"By and by to the office, where we sat all the morning; in great trouble to see the Bill this week so high, to above 4000 in all, and of them 3000 of the plague. Home, to draw over anew my will, which I had bound myself by oath to dispatch by to-morrow night; the town growing so unhealthy that a man cannot depend upon living two days."

August 31, 1665:

. . . . . "Every day sadder and sadder news of its increase. In the city died this week 7496, and of these 6102 of the plague. But it is feared that the true number of the dead this week is

near 10,000; partly from the poor that cannot be taken notice of, through the greatness of the numbers, and partly of the Quakers and others that will not have any bell ring for them. . . . . As to myself, I am very well, only in fear of the plague!" [Here we have an *estimated* mortality of 10[illegible]0 in a population of about 200,000, in a single week!]

September 6, 1665:

"To London, to pack up more things; and there I saw fires burning in the streets, as it is through the whole City, by the Lord Mayor's order. Thence by water to the Duke of Albemarle's; all the way fires on each side of the Thames, and strange to see in broad daylight two or three burials upon Bankside, one at the very heels of another; doubtless, all of the plague; and yet at least forty or fifty people going along with every one of them."

October 16, 1665:

"I walked to the Tower; but, Lord! how empty the streets are and melancholy, so many poor sick people in the streets full of sores; and so many sad stories overheard as I walk, everybody talking of this dead and that man sick, and so many in this place, and so many in that. And they tell me that, in Westminster, there is never a physician and but one apothecary left, all being dead; but that there are great hopes of a decrease this week; God grant it!"

October 29, 1665:

"In the street did overtake and almost run upon two women crying and carrying a man's coffin between them. I suppose, the husband of one of them, which methinks is a sad thing.

Shakespeare amidst such scenes, and then wonder at the frequent allusions to the plague! That would be doing scant reverence to his compassion and his genius.

The idea that the plague was due to a conjunction of the stars was still extant. This influence of the planets is spoken of by Ulysses when he says:

". . . . . but when the planets
In evil mixture to disorder wander,
What plagues and what portents,"
—*Troilus and Cressida*, I, 3.

In a treatise on the plague published by Lodge, in 1603, this idea is combatted, but the author falls into another fallacy by declaring on the authority of Avicenna that it is cured by an eastern hyacinth which is to be worn on the breast, or, preferably, is to be kept in the mouth. This hyacinth is also supposed to be able to resist all venoms. Autolycus in the Winter's Tale (IV, 4), referring to this custom of wearing charms against disease, declares: ". . . I have sold all my trumpery; not a counterfeit stone, not a riband, glass, pomander. . . ." Evidently Autolycus did not have the same faith in charms as Caius had in his kerchief. Besides the notion that the wind and the sun suck up disease from bogs, fens, and moors, and that the stars and planets "in evil mixture to disorder wander," we hear from the captain in Henry VI, Pt. II, IV, 1, that

"From their misty jaws (the jades)
Breathe foul contagious darkness in the air."

Among the agencies in the transmission of contagion the air holds first place. Consequently the Duke in Twelfth Night (I. 1) says of Olivia that "she purged the air of pestilence," and Portia pleads:

"What, is Brutus sick,
And will he steal out of his wholesome bed,
To dare the vile contagions of the night,
And tempt the rheumy and unpurged air
To add unto his sickness?"
—*Julius Cæsar*, II, 1.

That disease may be communicated by contact was not unknown to Shakespeare, for Falstaff tells us that

"Men take diseases one of another;
Therefore, let men take heed of their company."
—*Henry IV*, Pt. II, V, I.

We know that the clergy attributed morbus gallicus to divine visitation and that they were long accorded the benefit of their opinion after the laity were not. Astrologers naturally looked to the stars, but many physicians, notably Paré, took Falstaff's view (see Henry IV, Pt. II, II, 4). Physicians, crying in despair,

"'Tis contagious sickness;
Farewell all physick."
—*Henry VIII*, V, 2.

often fled before these epidemics, leaving their patients to the care of mountebanks or to those who gave baths. In such facts as these, rather than in the assertions that Shakespeare

"Did with unbashful forehead woo
The means of weakness and debility,"

lies the explanation for the many references to venereal diseases. The character of these references a personal perusal must reveal.

Among the therapeutic and diagnostic measures of the physicians of Shakespeare's time, purging, bleeding, and inspection of urine, or "water-casting," held a prominent place. They were frequently used to excess and are occasionally ridiculed in the plays of Shakespeare. In other instances their virtues are commended. Yet the picture presented to us by the many allusions, taken as a whole, agrees very well with that obtained by reading the professional literature of that day. Drastic purging was still practiced by the best physicians, but excessive bleeding and "water-casting" were not countenanced. Since it is much easier to obtain a good picture of the practices, as represented by Shakespeare, by direct quotations than by an attempted characterization, I shall adopt this method.

. . . "We are all diseased," (says the Archbishop in Henry IV),
"And with our surfeiting and wanton hours
Have brought ourselves into a burning fever,
And we must bleed for it."
—*Henry IV*, Pt. II, IV, 1.

The same advice is given by Biron in the lines:

"A fever in your blood! why then incision
Would let her out in saucers; sweet misprison!"
—*Love's Labor's Lost*, IV, 3.

According to Woodall's "Surgeon's Mate or Military and Domestic Surgery" a saucer or blood poringer held a trifle more than three ounces. Under the heading of "Blood Por-

ingers," Woodall cautions against too much bleeding as follows: "If the party be strong, except it be in case of Pleurisie, or some like urgent cause, I take less [than seven ounces]. I will rather offend in too little rather than in too much taking of blood away; for I have seen much hurt to have ensued by great quantity of blood taken away at one time." He also cautions against bleeding into basins as the German physicians did because of the inability of estimating accurately the quantity taken. This limit set by Woodall is but slightly exceeded by the First Sentinel in Coriolanus, when he threatens Menenius thus:

> **"I say, go; lest I let forth your half-pint of blood."**
>
> **—*Coriolanus*, V, 2.**

In the eighth of Dr. John Hall's "Select Observations on English bodies; or cures both empiricall and historicall performed upon very eminent persons in desperate diseases," etc., we find the following note:

> **"Mrs. Chandler of Stratford-upon-Avon, aet. 38, after long sickness and great flux of her courses, was cured thus: (A drastic purge was first administered.) After being let blood her courses stayed to admiration, and she became well. Three years after, being extremely weakened with the like flux in the time of her lying in that death was expected, she was cured by bleeding."**

King Richard's caution, "Our doctors say this is no month to bleed," (Richard II, I, 1) expresses well the popular superstition. People dared not be bled without consulting the stars. Those who could not pay for the services of astrologers consulted almanacs printed for that purpose. Even Queen Elizabeth herself had an astrologer in the person of Dr. John Dee, and the Rev. John Ward of Stratford-on-Avon, reports in his diary that "Nick Culpepper says a physitian without astrologie is like a pudden without fat." It is needless to say that the "puddin" usually contained fat.

In the sixteenth century to bleed meant also to purge. These were usually the initial procedures in case of fever and of many other affections. Macbeth, in speaking to the Scotch physician, bids him

> **. . . . . "Cast**
> **The water of my land, find her disease**
> **And purge it to a sound and pristine health, ...**
> **Pull't off I say.**
> **What rhubarb, senna, or what purgative drug,**
> **Would scour these English hence?"**
>
> **—*Macbeth*, V, 3.**

Purgation is usually spoken of in a figurative way as in this case. Other examples are:

> **"Methought she purged the air of pestilence!"**
>
> **—*Twelfth Night*, I, 1.**
>
> **"Let's purge this choler without letting blood."**
>
> **—*Richard II*, I, 1.**
>
> **. . . . . "I**
> **Do come with words as medicinal as true,**
> **Honest as either, to purge him of that humour**
> **That presses him from sleep."**
>
> **—*Winter's Tale*, II, 3.**

The nauseating character of the drugs used in general is repeatedly spoken of. That of those used to purge is likewise mentioned in the following homeopathic thought taken from the sonnets:

> **"As to prevent our maladies unseen**
> **We sicken to shun sickness when we purge."**
>
> **—*Sonnet*, 118.**

Hotspur, enraged at a certain dandy lord, contemptuously reports him as having said that

> **"It was a great pity, so it was,**
> **[That] villainous saltpeter should be digged**
> **Out of the bowels of the harmless earth,**
> **Which many a poor fellow had destroyed so cowardly."**
>
> **—*Henry IV*, Pt. I, I, 3.**

The exhausting nature of the excessive dosages of that time is brought out well by Coriolanus when he declaims against the assumption of popular rights after the people have disavowed him as consul. Coriolanus says that to assume these popular rights is

> **"To jump a body with a dangerous physic,**
> **That's sure of death without it."**
>
> **—*Coriolanus*, III, 1.**

The practice of prescribing from mere inspection of the urine had been so common that those who engaged in it were known as "water-casters" or "piddle doctors." This practice, which arose centuries before Shakespeare's time, resulted from restrictions upon the practice of medicine by monks, as a result of which they were no longer able to make personal visits to their patients. Hence they resorted to "water-casting." Treatises on "water-casting" seem to have been very popular. The "Urinal of Physik," written by Robert Recorde, who is usually credited with being the first English "piddle doctor," published in 1547, was reprinted in 1582, in 1599, and in 1665. This book, which in later editions went by the title, "The Judicial of Urines," gave pictures of the vessels used and subdivisions of urines with the prognoses in each case. In the Two Gentlemen of Verona, Speed apprises Valentine that . . . . "These follies are within you, and shine through you like the water in an urinal, that not an eye that sees you but is a physician to comment on your malady" (II, 1). Dr. Gideon Harvey, a physician contemporary with Shakespeare, quaintly describes a physician as giving the round toss to the urinal, or matula, to make the sediment subside. This urinal or matula was once the sign of the medical profession in Germany. One Notker, abbot of St. Gall in 1022, is said to have introduced the custom of having it carved on tombstones. Indeed, as late as 1450 Konrad von Sachsenhausen, the city physician of Frankfurt, had his tombstone similarly carved. Harris, in the Pharmacologia Anti-Empirica, tells of the impostures practiced by those who carried the specimens to the water-casters, and many amusing stories are told. He reports that Linacre, in order to show his contempt for the practice, often asked nurses and others to bring the shoe of the patient instead. One of the "quack" physicians, hearing of this, is said to have quickly proclaimed that he could diagnose and prognosticate all ailments from the odor of the shoe. As was the case with the

"piddle doctors," so also he undoubtedly did not always get the patient's shoe.

In Twelfth Night, III, 4, Fabian demurely advises Maria to "Carry his [Malvolio's] water to a wise woman" in order to determine whether Malvolio is bewitched or not. The value of this practice to the patient is probably estimated correctly by the page, who replies to Falstaff's question, "Sirrah, you giant, what says the doctor to my water?", with the words, "He said, sir, the water itself was a good healthy water, but for the party who owned it, he might have more disease than he knew for" (Henry IV, Pt. II, I, 2). Since, according to the Fifth Henry, chapter six, there were only twelve regular surgeons and probably a somewhat larger number of regular physicians in all London at the time of Henry VIII, it would be unjust to visit all this abuse on the regular "practisers of physic." As a class, physicians were, no doubt, urine inspectors. But a motley group composed the medical profession of that day. Since the London proper of Henry VIII had a population of about 150,000, it is evident that a few dozen regular doctors could not supply the need. Consequently there must of necessity have been many "irregulars." However, it would be unjust to conclude that all those who were not licensed by "the congregated college" were unsuccessful or even incapable practitioners. There are many evidences to show that the power of the Royal College of Physicians was for a time almost absolute and that it was sometimes arbitrarily used. But we have the testimony of Dr. Caius, the founder of Caius College and second president of the Royal College of Physicians, as to who composed the medical profession of that day. Dr. Caius enumerates "simple women, carpenters, pewterers, braziers, soap-ball sellers, apothecaries, and avaunters themselves," among physicians. Fifty years after this, Cotta, in his "Short Discoverie," gives a similar summary containing midwives, cooks, priests, witches, conjurers, jugglers, and fortune-tellers." Individuals were frequently licensed to practice specific things only, as for example, to cure fistula, extract or treat cataract, or to operate on hernia or hare-lip. However, the Royal College of Physicians made itself felt. The signs of physicians were to be displayed at their residences only and in consequence of a statute framed by Linacre, apothecaries were restrained from carrying the urine of their patients to a doctor and prescribing for the patient in consequence of the doctor's opinion. This statute was followed by another which forbade doctors to pronounce on any disorder from an examination of the urine alone.

We are all familiar with the freedom with which Shakespeare used Holinshed for the tragedies and historical plays. Whether it be the Palamon and Arcite of Chaucer which is to be transformed into the Two Gentlemen of Verona, the Tale of Troy which is to live again in Timon of Athens, or the Italian stories of Boccaccio and Bandello which are to be reinvigorated, we always find the master hand of Shakespeare moulding the crude materials of the sources according to the dictates of his unequalled dramatic genius. The same freedom taken with facts of history was taken with those of medicine. Many things have been adopted bodily, others have been greatly modified to suit the dramatic and artistic needs of the plays. Consequently we find anachronisms, inaccuracies, exaggerations, and contradictions.

"A letter for me?" asks Menenius, "It gives me an estate of seven years' health, in which time I will make a lip at the physician; the most sovereign prescription in Galen is but empiricutic, and, to this preservative, of no better report than a horse drench" (Coriolanus, II, 1). Coriolanus lived four to three hundred years before Galen. Hence Menenius could hardly make a lip at Galen. Besides these words are not characteristic of the times. To "make a lip at Galen" was not the attitude of Shakespeare's time, even if a layman might have done so with impunity. Not so a physician, however. This is shown by the following entry from the Roll of the Royal College of Physicians, of London (2d Edition, Vol. I, p. 62, 1878): "On his acknowledgment of error and humble recantation, signed with his own hand, he was received into the College." The person disciplined was Dr. John Geynes, who was cited before the College in 1559 for impugning the infallability of Galen. This was but fifty years before Coriolanus was written.

"Who keeps the tent now?" asks Patroclus of Thersites. The reply is, "The surgeon's box or the patient's wound." The time of the tragedy of Troilus and Cressida is 1184 B. C. Consequently we do not expect to hear of a surgeon's box or of the use of a tent. A similar anachronism is the use of the doctor's title in Macbeth several hundred years before the time in which it came into use. Other errors are the use of the kerchief of Shakespeare's day with its medical significance in the Roman times of Julius Cæsar, and the presence of symptoms of quickening by the second month. Little significance should, however, be attached to these errors. Many may be intentional. Besides we must allow for poetic license. These things must be regarded as we regard the introduction of cannon in King John and in Macbeth. This made the warfare of these plays more intelligible.

Instances of extravagant expressions are numerous, and are frequently accounted for by the dramatic situation or the character of the speaker. No one would take Fabian seriously when he implies that he can tell a madman by inspecting his brain; or Hamlet, when he determines the question of his sanity by the state of his pulse; or the King in All's Well That Ends Well, when he says that Helena has repealed the banished sense of his hand. Other examples are Gloucester's assertion that he was born with teeth; Helena's cure in two days of a fistula which the "congregated college" had declared incurable; and Lafeu's boast that he has "seen a medicine"

> "That's able to breathe life into a stone,
> Quicken a rock, and make you dance canary
> With sprightly fire and motion."
>
> —*All's Well That Ends Well*, II, 1.

In this class of references we must also place the threat of ovariotomy by the irate Antigonus in the Winter's Tale, II, 1.

We must not take these things literally any more than we take Shakespeare literally when he makes Romeo declare, "Hang philosophy unless philosophy can make a Juliet." Indeed, if we take everything in the plays of Shakespeare literally, we rob the great Linnaeus of the discovery of sex in plants, for, in the Winter's Tale, Perdita speaks of . . . . "pale primrose that die unmarried." This apparent reference to sex recurs more clearly in Romeo and Juliet and in Midsummer Night's Dream in the following words:

> "Among fresh female buds
> Shall you this night inherit at my house,"

and

> "The female ivy that enrings the barky fingers of the elm."

I am fully aware that there are those who have magnified Shakespeare's insight until they have claimed that he foresaw advancements in science which only the great scientists of the twentieth century have achieved. Such assertions, however, are interesting mainly as an index to a large part of the literature on this subject. It would be doing a great wrong to the truly learned physicians and surgeons of the sixteenth century and to their illustrious predecessors, to claim that the characteristics of the medicine of the plays of Shakespeare are those of the medicine of Woodall, Riolan, Botal, Harvey, Caius, Banester, Linacre, Paré, and many others. There are, it is true, some points of similarity, yet little can be found in the medicine of the dramas of Shakespeare indicative of the learning of these men. It is the popular, and the general rather than the special and minute, that is found in Shakespeare. The picture we obtain is, in the main, that which could easily be obtained from the life of that time by a layman of *such extraordinary genius* as Shakespeare's. The wonderfully accurate descriptions of death and old age are eloquent testimonials of his powers of observation, expression and portrayal. It would be useless to try to find parallels to them in the professional treatises of that time or of any other time. Be their professional attainments what they might, lacking Shakespeare's genius, physicians were, and must remain, unable to write as wrote the great master of English. To be sure, there are certain internal evidences tending to show that the medicine of the plays of Shakespeare is, in some things at least, fully abreast of that of the professional treatises of the times. But they are too few and inadequate to characterize it as a medicine based on clinical experience and anatomical knowledge. In short, the medicine of the plays of Shakespeare is Hippocratic medicine modified by Galenism, with a touch of Paracelsus. These elements are all represented in the best treatises on medicine of the sixteenth century. The characteristics of the medicine of Shakespeare are, in a manner, those of the medicine of the best physicians contemporary with him. It is not, however, a purposeful medicine based on medical training and clinical experience, but incidental, the product of a world genius, and therefore a greater tribute to his enduring fame.

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[2] All references to the plays of Shakespeare are based on the International Edition of the University Society of New York. Only a partial list of references to the literature on the medicine of Shakespeare has been given.

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THE VARIOUS TYPES OF CARCINOMA CERVICIS UTERI: THE CHANGES THEY UNDERGO WITH THE PROGRESS OF THE DISEASE AND THEIR CLINICAL SIGNIFICANCE

By JOHN A. SAMPSON, M. D.,

Gynecologist to the Albany Hospital, Albany, N. Y.; Clinical Professor of Gynecology, Albany Medical College.

(From the Gynecological Department, Johns Hopkins Hospital, Baltimore, Md.)

Experience has taught us that the clinical course of cancer of the uterine cervix is usually rapid; the patients rarely live over three years, about three-quarters of them die within two years, and one-third within one year, after the first manifestation of the disease. Bleeding in some form is usually the first evidence of this condition; this is sometimes not present until late in the course of the disease, but if absent, usually some other symptoms such as a watery or foul discharge should call attention to the growth. In a small percentage of the cases all symptoms referable to the growth are absent until after it has extended beyond all possibilities of a cure. Bleeding or a blood-tinged discharge was present in about ninety-three per cent of 412 cases of cervical cancer admitted to Dr. Kelly's clinic at the Johns Hopkins Hospital, and in over sixty per cent of these cases there was a history of neglected uterine bleeding for over six months. When we bear in mind the usual rapid course of the disease, we can readily understand why hysterectomy so seldom cures this condition, why it is important to make an early diagnosis and also why the patient should be operated upon as soon as possible after making this diagnosis.

We know that only a small percentage of all cases have been "operable," and we also have learned that a small percentage of those operated upon can be cured, but believe that all could be cured if the entire diseased condition could be removed and implantation avoided. The importance of an early diagnosis is very urgent, and fortunately it is possible in a large percentage of the cases if women only realized the curability of this condition in its early stages and we, the physicians, would ascertain without delay, in every instance, the cause of uterine bleeding or of any other symptom referable to the uterus.

Two things then are very essential; first, the education of women along these lines, and second, our own education in order that we may better understand the pathological changes caused by this disease and their clinical manifestations.

All women should fully realize that any uterine bleeding or other symptoms referable to the pelvic organs may be indicative of some slight trouble, which may not need any attention or can be easily remedied if it does, or on the other hand, that it may be the first manifestation of cancer which, if operated upon in its incipiency, should be cured in a large percentage of the cases. This bleeding may be slight, "only a show" appearing at irregular intervals as on exertion, or after coitus, or after using a douche or straining at stool. In other cases the bleeding may be slight but constant, the patient noticing that her clothes are slightly soiled on taking them off at night. Sometimes the bleeding is more profuse, so that it may appear like a prolonged menstruation, an irregular menstruation or a return of the flow after the menopause. In still other cases there may be severe hæmorrhages.

All physicians should bear in mind that there are various types of the growth which may alter the clinical picture of the disease, and the various stages of each type may also present different clinical features.

It seems appropriate to study these various types and the changes they undergo during the progress of the disease, in order that we may understand the clinical manifestations of the disease, its diagnosis and the indications for its treatment.

While Resident Gynecologist at the Johns Hopkins Hospital, I began a careful study of twenty-seven specimens removed by the more radical abdominal operations and also one autopsy specimen from a patient with cervical cancer, dying from cerebral embolism due to an acute endocarditis. Fortunately only a few of these cases had been curetted and an excellent opportunity presented itself to study the various types and the changes they undergo as the disease progresses. A drawing, to measure, was made of each specimen removed and also one of the vaginal portion of the cervix and in several instances plaster casts of the latter were made. The specimens were hardened in 4 per cent formalin and, after hardening, a sagittal slice about 2 mm. in thickness was removed, thus dividing the specimen into two halves. This slice (either as a whole or else divided if too large) was imbedded in celloidin, cut and stained as a microscopical section, thus giving a stained sagittal section of the entire uterus, demonstrating the relation of the disease to the cervix and its method of extension through the tissues of the cervix, and in a few instances into the fundus. Cross sections were then made of each half of the specimen and by this incomplete series the invasion of the parametrium was studied. From the sagittal sections and the series (incomplete) of cross sections, the growth was reconstructed thus demonstrating its relation to the parts involved. Cancer was either found or its existence excluded from the pelvic lymph nodes removed.

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CLASSIFICATION OF CANCER OF THE UTERINE CERVIX.

I. *Histological.*—The vaginal portion of the cervix is normally covered by stratified epithelium which is directly continuous with that of the vagina and usually ends at the external os but may extend up into the cervical canal for varying distances, which is especially true as women grow older. The cervical canal, on the other hand, is lined by high cylindrical cells which generally meet the stratified epithelium at the external os, but may extend over the vaginal portion of the cervix. Cancer arising from the stratified epithelium, no matter the place of origin, whether from the vaginal portion or within the cervical canal, is known as *squamous cell carcinoma.* Likewise cancer arising from the cylindrical epithelium or glands of the cervix, no matter its place of origin, is known as *cylindrical cell* or *adeno-carcinoma.*

II. *Topographical.*—As we may group all forms of uterine cancer according to whether they arise in the body or in the cervix, in like manner we may classify cervical cancer according to its origin whether in the *vaginal portion* of the cervix, or within the *cervical canal.*

III. *Morphological.*—Irrespective of the situation of the growth or its histological structure, we may group it according to its morphology. We do not know why, in one case, the growth seems to "evert" giving rise to a papillary or cauliflower mass, or in another, apparently the same type of growth may "invert" forming a nodule or mass of cancerous tissue in the cervix with but very little evidence of the disease on the surface. The malignant process may be circumscribed in one instance, and apparently the same type of growth may be diffusely scattered throughout the cervical tissue in another. Intermediate forms and sometimes both processes are present in the same specimen. Apparently in the progress of the disease the growth may sometimes pass from one morphological type into the other. We can, however, frequently make the following classification:

1. Everting or vegetative (synonyms—cauliflower, papillary and proliferating);

2. Inverting or infiltrative (synonyms—nodular, ulcerative and parenchymatous).

In some cases the cancer cells predominate and the stroma forms a very small part of the tumor, as a result the tumor may feel soft, hence the term *medullary,* and it may early become necrotic and portions of it slough away. The process less frequently invades the cervical tissue in a diffuse manner forming a growth in which the stroma predominates, the so-called "scirrhus" cancer, which may retain its form for a long period of time. Specimens are encountered which cannot be included in the above classification and which should be looked upon as "exceptions" or isolated cases until we learn more about them and either discover, on further study, that they belong in one of the above groups, or that it may be necessary to form new groups for them.

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Squamous Cell Carcinoma—Vaginal Portion of Cervix—Everting or Vegetative.

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The inverting or infiltrating type also apparently begins as a proliferation of the epithelium of the vaginal portion of the cervix, and here the papillary formation is absent or plays a minor part. The growth seems to invert itself into the

THE VARIOUS TYPES OF CARCINOMA CERVICIS UTERI: THE CHANGES THEY UNDERGO WITH THE PROGRESS OF THE DISEASE AND THEIR CLINICAL SIGNIFICANCE

By JOHN A. SAMPSON, M. D.,

Gynecologist to the Albany Hospital, Albany, N. Y.; Clinical Professor of Gynecology, Albany Medical College.

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Experience has taught us that the clinical course of cancer of the uterine cervix is usually rapid; the patients rarely live over three years, about three-quarters of them die within two years, and one-third within one year, after the first manifestation of the disease. Bleeding in some form is usually the first evidence of this condition; this is sometimes not present until late in the course of the disease, but if absent, usually some other symptoms such as a watery or foul discharge should call attention to the growth. In a small percentage of the cases all symptoms referable to the growth are absent until after it has extended beyond all possibilities of a cure. Bleeding or a blood-tinged discharge was present in about ninety-three per cent of 412 cases of cervical cancer admitted to Dr. Kelly's clinic at the Johns Hopkins Hospital, and in over sixty per cent of these cases there was a history of neglected uterine bleeding for over six months. When we bear in mind the usual rapid course of the disease, we can readily understand why hysterectomy so seldom cures this condition, why it is important to make an early diagnosis and also why the patient should be operated upon as soon as possible after making this diagnosis.

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tissues of the cervix and usually gives rise to a more or less circumscribed mass of cancerous tissue. Usually the stroma plays a small part in the structure of the tumor and the epithelial cells predominate, the so-called medullary cancer; less frequently, however, the disease process invades the cervical tissue in a diffuse manner forming a growth in which the stroma predominates, the so-called scirrhus cancer. The starting place of the new growth varies in different cases. In the one shown in Figs. 5 and 6, it apparently started in the centre of the anterior lip near the junction of the squamous and cylindrical epithelium, while in the case shown in Figs. 7 and 8, it apparently started in a similar place of the posterior lip. On the other hand, in the case shown in Figs. 9 and 10 there is possible a double focus, *i. e.*, the simultaneous appearance of the growth in each angle of the external os.

As the disease progresses it invades the deeper tissues of the cervix, extending directly in and usually avoiding the cervical canal. Sometimes a large mass of cancerous tissue will be found, hence the name "nodular cancer." In the specimen shown in Figs. 5 and 6 the entire anterior wall of the cervix had apparently become involved before ulceration had taken place. More often, however, the processes of invasion, necrosis and ulceration go on together as shown in Figs. 7, 8, 9, 10, 11, and 12, hence the term "ulcerative" cancer. As the disease progresses further and replaces the tissues of the cervix, the central core including the cervical canal frequently sloughs away and the cervix is converted into a crater-like cavity lined by necrotic cancerous tissue as shown in Figs. 13 and 14. The clinical manifestations of this type depend on the amount of necrosis and ulceration. A growth which becomes necrotic early in its course would give rise to symptoms sooner than one which did not. In the patient shown in Figs. 5 and 6, where there was an extensive cancerous mass with but very little necrosis, bleeding had been noticed but seven weeks before the operation, while in the one shown in Figs. 9 and 10 bleeding had been present for over eight months. Yet in the latter case the growth was small and without metastases, while in the former, the growth was large and metastases had occurred. We must infer, that in the patient with a small growth and symptoms for eight months either the disease progressed very slowly or the symptoms appeared very early, and in the other with a large growth and bleeding for only seven weeks, either the cancer grew very rapidly or else the symptoms did not appear until late. The patient, whose uterus is shown in Figs. 7 and 8 had known of the ulcerated condition of the cervix for six months and yet one sees that the primary growth was very small; on the other hand, metastases to the pelvic lymphatics had already occurred. In the case shown in Figs. 11 and 12 the diagnosis was made on examining the patient for symptoms arising from a pelvic inflammatory disease which was associated with the cancer, but independent of it, and symptoms referable to the cancer had been of but ten days' duration. The disease had metastasized at the time of the operation and the patient later died from recurrence due to some of the cancerous pelvic lymph nodes which had not been removed at the operation. On the other hand, the uterus shown in Figs. 13 and 14 had been bleeding for over six months before the operation.

It can readily be seen in this type of cancer, that if the growth is rapid or necrosis is delayed the disease may easily pass beyond the curative stage before it is detected. On the other hand, if the growth is slow and especially if necrosis occurs early, the diagnosis may be made while the disease is still local. *Unfortunately there is no relation between the extent of the diseased process and the duration of the symptoms, i. e.*, the disease may be extensive and the symptoms of short duration and also the disease may be early and it may have manifested itself, clinically, for a long time.

In the further progress of the disease the bladder may be involved anteriorly as shown in Fig. 15 and later a vesico-vaginal fistula may appear. In the posterior extension of the disease the cul-de-sac may become obliterated and the rectum become invaded as shown in Fig. 16 or the rectum may become invaded through the posterior vaginal wall. As a result of the posterior extension of the disease a recto-vaginal fistula may appear. In the lateral extension of the disease the ureters soon become surrounded and compressed, or if it extends both posteriorly and laterally, the sciatic nerves may become invaded and cause excruciating pain. Fortunate indeed is the woman when the ureters become compressed before the formation of the above mentioned fistula or invasion of sensitive nerves, for the resulting renal insufficiency benumbs the sensibilities and favors a terminal infection.

It can be seen that the inverting or infiltrating variety is more malignant than the everting type and is also of more frequent occurrence. Unfortunately it may not give rise to any symptoms until after it has extended beyond the uterus. Its detection by inspection or palpation, unless ulceration is present, is also more difficult than in the everting type.

Squamous Cell Carcinoma—Vaginal Portion of Cervix—Both Everting and Inverting.

As has been previously stated, both types of growth may be present in the same specimen and in fact usually are, for the one name or the other is given to the prevailing type. We have papillary projections from the floor of the ulcer or sides of the craterous cavity and every everting type eventually has an infiltrating base. So the classification is somewhat artificial, but is of importance as a help in understanding the various forms of growth. In the case shown in Figs. 17 and 18, which probably belongs in the last group mentioned, the disease apparently began as an infiltrating form but burst its outer shell and assumed the everting type. This patient had been bleeding for three months. Notice that the growth apparently began in the posterior lip, invaded the deeper tissue and through it encircled the cervical canal.

Squamous Cell Carcinoma—Cervical Canal—Everting.

Squamous cell carcinoma arising within the cervical canal

may also be grouped into the everting and inverting forms; the everting form may fill the canal or even protrude through the external os into the vagina. In Figs. 19 and 20 is shown the shrunken and retracted cervix so characteristic of the growths developing in the cervical canal and in addition a portion of the growth is protruding from the external os as a papillary outgrowth. The sagittal sections show that a pyometra had resulted from the occlusion of the cervical canal by the growth. This is the only instance in the twenty-eight cases where there was any resemblance to an everting type of growth arising from the cervical canal. A history of three months' bleeding was present and the growth had invaded the parametrium, and metastases were found in the pelvic lymph nodes.

Squamous Cell Carcinoma—Cervical Canal—Inverting.

The same changes occur in the inverting type of growth starting in the cervical canal as in the similar type of growth arising from the vaginal portion of the cervix. However there is this difference. This form of growth, arising from the vaginal portion of the cervix, nearly always extends by invading the deeper tissue of the cervix rather than spreading over the mucous membrane and up the cervical canal; as a result the cervical canal may be entirely surrounded by cancer and yet remain intact until late in the course of the disease, and finally the central core including the canal may slough away. On the other hand, in cancer arising within this canal the mucosa of the canal is the first tissue attacked. From the mucosa, the cancer spreads on all sides into the cervical tissue. We nevertheless see the changes caused by infiltration and ulceration, and finally the cervix is converted into a thin shell lined by cancerous tissue just as in the other type. In the advanced stages the picture may be such that it is impossible to state whether the disease started within the canal or from the vaginal portion of the cervix. Frequently, however, the vaginal portion of the cervix may not be invaded—even in cases of extensive cancer developing within the canal (see Figs. 25 and 26). In Figs. 21 and 22 is shown a very early case in which the disease had started within the external os and after spreading over the surface of the cervical canal, had invaded the deeper structures on all sides, and yet there has been but little change in the vaginal portion of the cervix. A little puckering of the anterior lip, caused by the lower edge of the growth just within the external os, was present. In the specimen shown in Figs. 23 and 24 the disease is further advanced, more of the cervical tissue has been invaded and also the tissue beneath the mucosa of the vaginal portion of the cervix, thus causing a retraction and puckering of the latter. The specimen shown in Figs. 25 and 26 represents a still further stage of the disease where the entire central portion of the cervix had sloughed away. Note, however, that there has been but very little involvement of the vaginal portion of the cervix, the latter being retracted, shrunken, and puckered, but its mucosa, for the most part, is intact.

In the specimen shown in Figs. 27 and 28 the growth had invaded the cervical tissues in a diffuse manner, the so-called scirrhus type, and had undermined the mucosa covering the vaginal portion of the cervix causing the former to slough away from the greater portion of the cervix, there still being an irregular border of intact mucosa about its outer margin. The growth had also invaded the deeper tissues of the vagina on all sides of the cervix without involving its mucosa.

The symptomatology varies in these cases and there is no definite relation between the duration of the symptoms and the extent of the disease. In the very early case shown in Figs. 21 and 22 a thin watery discharge had been present for three years, and bleeding was first noticed only a few days before the patient came to the hospital. The patient represented in Figs. 23 and 24 had been bleeding for seven months, and the one represented in Figs. 25 and 26 had been bleeding for eighteen months, but here a uterine polyp was found which may have also caused bleeding. Bleeding had been present for two and a half years in the patient represented in Figs. 27 and 28.

The diagnosis of this type presents all the difficulties of the preceding one, with the additional feature that the disease starts within the cervical canal. The disease seems, rarely or only very late, to appear on the vaginal surface of the cervix. However, there is one very important feature which aids in the diagnosis and that is the alterations in the vaginal portion of the cervix caused by the disease invading its deeper tissues. The vaginal portion of the cervix becomes indurated, and with necrosis, the cervix becomes retracted, puckered, and the vaginal mucosa covering it, is thrown into folds. This induration, retraction, and puckering of the vaginal portion of the cervix is as characteristic of this form of cancer, as is the retraction of the skin or the nipple characteristic of the mammary cancer lying beneath. The prognosis in these cases is probably about the same as in the similar type arising from the vaginal portion of the cervix.

Squamous Cell Carcinoma—Inverting—Starting Place Undetermined.

In very advanced cases it may be impossible to determine the origin of the growth. In the two specimens shown in Figs. 15 and 16 the disease apparently started from the vaginal portion of the cervix and not from within the canal, still this cannot be definitely stated. As previously emphasized, it is remarkable how extensive the disease may be in a growth starting within the canal and the vaginal portion of the cervix may not yet have been destroyed. In the specimen shown in Figs. 29 and 30 it is impossible to definitely state the origin of the growth (classified under inverting type arising from the vaginal portion of the cervix), whether from the vaginal portion of the cervix, the vagina, or just within the external os. There was a marked reaction on the part of the surrounding tissue causing an infiltration of eosinophiles, so marked as to greatly obscure the malignant growth. As shown, the cervix and vagina are both involved; in addition

the parametrium was invaded by direct extension and by metastases, and metastases were present in the pelvic lymph nodes. The bleeding was of six months' duration.

Adeno-Carcinoma—Uterine Cervix.

This, as we know, may arise from the vaginal portion of the cervix or from within the cervical canal and may be everting or inverting. The specimen shown in Figs. 31 and 32 now appears as an infiltrating type starting within the cervical canal. There was a history of bleeding for seventeen months, and seven months before her admission to the hospital a tumor was removed from the cervix. This suggests that there was probably present, at that time, a fungating growth protruding from the external os, *i. e.*, it originally manifested itself as an everting type arising from the cervical canal. In Figs. 33 and 34 is shown a specimen of adeno-carcinoma obtained at autopsy, the patient died of cerebral embolism from acute endocarditis. Metastases were found in the lungs, liver, and in the thoracic, abdominal, and pelvic lymphatics. There was a history of bleeding for six months. The growth is apparently of the inverting type starting from the deep cervical glands, as the mucosa lining the canal was normal in places. It may have originated in the left corner of the vaginal portion of the cervix, but this does not seem probable. In Figs. 35 and 36 is represented a third case of adeno-carcinoma of the inverting type starting within the cervical canal and causing occlusion of the canal, with a resulting pyometra. The retracted puckered cervix is well shown, and this is covered by epithelium having the histological appearance of squamous cell carcinoma, thus suggesting the presence of both adeno-carcinoma and squamous cell carcinoma in the same specimen. There was a history of bleeding for seven months

Figs. 37 and 38 represent a specimen of apparent adeno-carcinoma starting within the cervical canal and suggest a double focus. The growth was apparently very early, symptoms of bleeding having been manifest for only three weeks. It, however, recurred in a few months after the operation and soon filled the pelvis. The recurrence manifested itself first in the vaginal vault and suggested that an implantation of cancer cells had taken place during the operation.

THE CLINICAL SIGNIFICANCE OF THE VARIOUS TYPES OF GROWTHS.

The following classification of cancer of the uterine cervix has been made:

I. Histological: (1) Squamous cell carcinoma. (2) Cylindrical cell or adeno-carcinoma.

II. Topographical: (1) Those arising in the vaginal portion of the cervix. (2) Those arising in the cervical canal.

III. Morphological: (1) Everting or vegetative (synonyms—cauliflower, papillary, and proliferating). (2) Inverting or infiltrating (synonyms—nodular, ulcerative, and parenchymatous).

In the majority of the cases we can employ the above classification. The histological picture is usually definite, but at times the diagnosis may be in doubt; in the case shown in Figs. 35 and 36 both adeno-carcinoma and the squamous cell variety are present. A difference of opinion has been expressed by different pathologists as to the diagnosis in Figs. 37 and 38. The topographical diagnosis is not always evident. It is remarkable how extensive a growth, arising from the vaginal portion of the cervix and invading the deeper tissues of the cervix, may be, and yet the cervical canal may be intact or very little involved, as shown by the sagittal sections in Fig. 12. Likewise one may have a very advanced growth arising within the cervical canal and the vaginal portion of the cervix may be intact, or slightly involved, or else invaded only from the deeper cervical tissues (see Figs. 14 and 16). However, in many of the very advanced cases it is impossible to state where the growth arose and the same is true of a few of the early or operable ones. In considering the morphology of the growth some are definitely everting, as shown in Figs. 1, 2, 3, and 4, and others are just as definitely inverting as shown in Figs. 5, 6, 7, and 8, but in others both processes may be present in the same specimen and also, in the progress of the disease, the growth may pass from one type to another.

The Clinical Significance of Squamous Cell Carcinoma—Vaginal Portion—Everting.

Four of the twenty-eight specimens were of this variety and possibly one or two others included in the next group. In only one of the four cases was the parametrium involved by cancer and in two of the cases, in which the pelvic lymph nodes were studied, cancer was not found. In one of the four cases there was a history of neglected uterine bleeding for over six months and in the other three for over five.

The above suggests that this is one of the most favorable types of growth, invading the surrounding tissue slowly and soon giving rise to symptoms. It is so situated and of such an appearance and structure that it may be easily diagnosed on inspection or palpation.

The Clinical Significance of Squamous Cell Carcinoma—Vaginal Portion—Inverting.

This is apparently the most frequent type of the squamous cell variety, occurring fifteen times in the nineteen cases of cancer arising from the vaginal portion of the cervix. It is apparently as malignant or even more malignant than the same variety arising within the canal, for it spreads by directly invading the deep tissues of the cervix rather than by extending over the surface, as up the cervical canal or over the vagina. It also soon reaches the parametrium, and metastases may occur even before the latter has become invaded by the tumor. The parametrium was involved, either by direct extension or metastases, in eleven of the fifteen cases. Some of the lymph nodes were studied in fourteen cases and were found involved in six, and in two of these six cases no evidence of cancer was found in the parametrium. In seven of

FIG. 1.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix, Everting or Vegetative (Gyn. Path. No. 7601).

Patient 37 years old; 4 children (youngest 9 years). A bloody discharge had been present for five months and a severe hæmorrhage occurred, while straining at stool, three weeks ago. Pain was probably due to adhesions from pelvic inflammatory disease. General condition was excellent.

The movements of the uterus were limited by pelvic adhesions from a previous pelvic inflammatory disease. The parametrium was apparently free.

Vaginal portion of the cervix (natural size) shows that the posterior cervical lip has been replaced by an everting papillary growth which bled on palpation. The growth had begun to spread over the posterior vaginal wall.

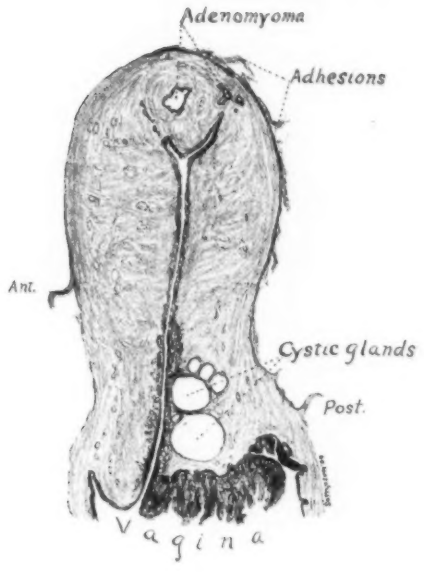

FIG. 2.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 1.

The papillary growth is gradually absorbing the tissue of the posterior cervix lip and is beginning to spread over the posterior vaginal wall and up the cervical canal occluding the openings of some of the cervical glands, and thus causing retention cysts.

The adhesions are shown on the surface of the uterus and an adenomyoma is present in the fundus. Cancer was not found in the parametrium or in the pelvic lymph nodes removed.

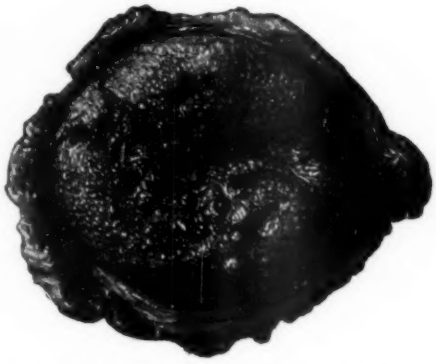

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FIG. 3.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix, Everting or Vegetative (Gyn. Path. No. 8155).

Patient 30 years old; 1 child (15 years). More or less constant bleeding had been present for five months, and was the only symptom. General condition was excellent.

The uterus was freely movable and parametrium was apparently normal.

Vaginal portion of the cervix (natural size) shows that both lips have been replaced by an everting papillary growth which bled easily, on palpation.

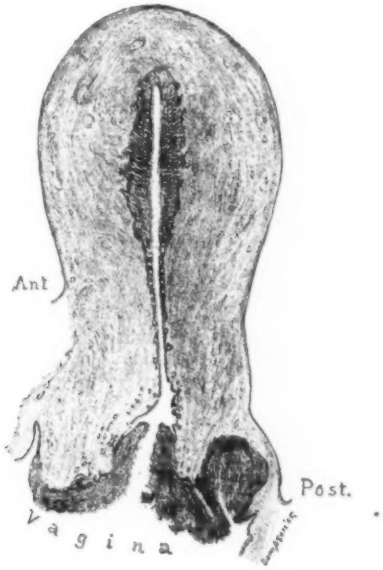

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FIG. 4.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 3.

The papillary outgrowth has covered the entire vaginal portion of the cervix and has invaded the deeper tissues at the junction of the posterior lip and the vagina. Cancer was not found in the parametrium (the pelvic lymph nodes were not removed).

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FIG. 5.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting or Infiltrating (Gyn. Path. No. 6669).

Patient 62 years old; 2 children (45-43 years); menopause nine years ago. Bleeding at irregular intervals had been present for seven weeks, usually when straining at stool and at one time amounting to a severe hæmorrhage. A very profuse watery discharge, not offensive, had been present for four months. Pain was not present. General condition was poor, hæmoglobin 68 per cent.

Uterus was freely movable and parametrium apparently normal.

Vaginal portion of cervix (natural size) shows a markedly hypertrophied and indurated anterior cervical lip, the center of which has broken down, forming an ulcer lined by friable necrotic tissue, the posterior lip has become atrophied and the canal displaced backwards.

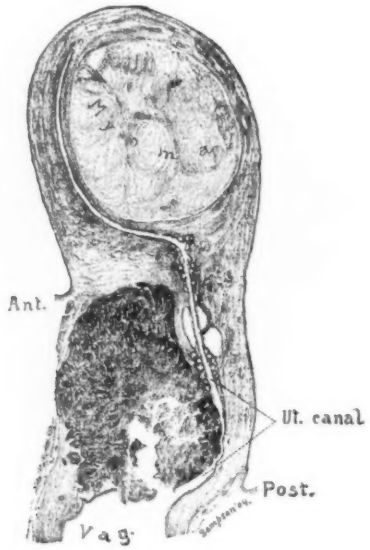

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FIG. 6.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 5.

The growth has formed a mass of cancerous tissue involving the anterior wall of the cervix and extending as high as the internal os. Note that the cervical canal has just begun to be involved and that it has been displaced backwards and that the fundus, vagina, and posterior wall are free. A submucous myoma is present in the posterior uterine wall.

A metastasis was found in a parametrial lymph node, the pelvic lymph nodes removed were free.

FIG. 7.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting or Infiltration (Gyn. Path. No. ——).

Patient 49 years old; 3 children (youngest 21); menopause one and a half years ago. No bleeding, but a profuse discharge requiring the use of a douche had been present for nine months and six months ago her physician recognized "an ulcer" on the cervix, but did not suggest a diagnosis of cancer until two weeks before operation. Pain in the left side (due to metastases) was very severe. General condition was only fairly good.

Uterus was freely movable and parametrium was apparently normal. Vaginal portion of the cervix (natural size and not curetted), shows a superficial ulcer situated in the outer half of posterior lip, edges undermined, and base firm, did not bleed on palpation. Tissue just about the ulcer was indurated.

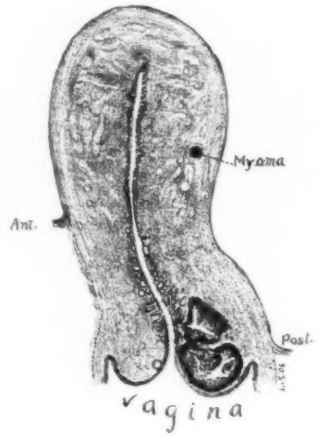

FIG. 8.—Stained Sagittal Section of the Uterus (slightly reduced) shown in Fig. 7.

A small primary growth is situated in the tissue of the posterior wall of the cervix (section is taken just mesial to the ulcer in the cervix). This section shows a characteristic feature of this type of growth and that is it extends by the invasion of the deeper cervical tissues and not by spreading, over the surface; also seen in the preceding case.

Cancer was not found in the parametrium, but the pelvic lymph nodes of the left side of the pelvis were extensively diseased.

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FIG. 9.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting, Possibly a Double Focus (Gyn. Path. No. 6848).

Patient 58 years old; 13 children (30-9 years); menopause two and a half years ago. Only symptom had been a slight but constant blood-tinged discharge of eight months' duration following a slight hæmorrhage at the onset. Condition was good, hæmoglobin 90 per cent.

Uterus was freely movable and parametrium was apparently normal.

Vaginal portion of the cervix (natural size and not curetted) shows two small superficial ulcers, situated in each corner of the external os and spreading over the outer surface of the cervix. The bases of these ulcers are covered by friable tissue which bled easily on palpation.

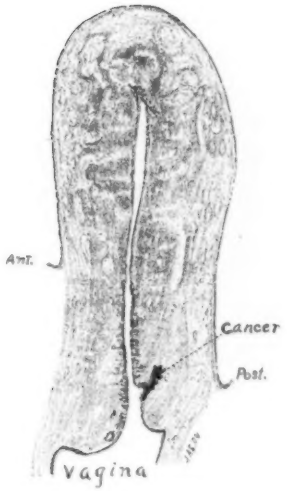

FIG. 10.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 9.

A small cancerous area is present in the posterior lip which as an "isthmus" unites the two areas of cancerous tissue situated on each side. Cancer was not found in either the parametrium or pelvic lymph nodes.

A very early case, but clinically of eight months' duration.

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FIG. 11.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting; Extensive (Gyn. Path. No. 7077).

Patient 36 years old; 1 child (age ?). History was unsatisfactory. Bleeding had been present for only a few days, but probably the patient had been curetted a month before her admission. Pain, of seven weeks' duration, was probably due to the extensive pelvic inflammatory disease which was present. General condition was excellent, hæmoglobin 100 per cent.

Movements of the uterus were restricted by pelvic adhesions. Parametrium on left side felt slightly indurated.

Vaginal portion of the cervix (natural size, curetted ? a month ago) shows a necrotic ulcer involving the entire posterior lip and the outer portions of the anterior, which bled easily on palpation.

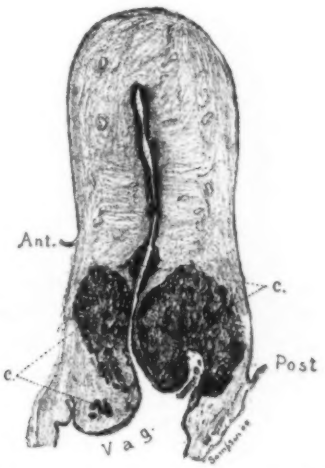

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FIG. 12. Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 11.

The growth has invaded the tissues of the cervix and has surrounded the cervical canal, in places involving it. The growth stops at the internal os.

The parametrium of the left side was invaded by direct extension and that of the right by metastases. Metastases were also found in the pelvic lymph nodes of the left side.

An extensive growth with a clinical history of short duration.

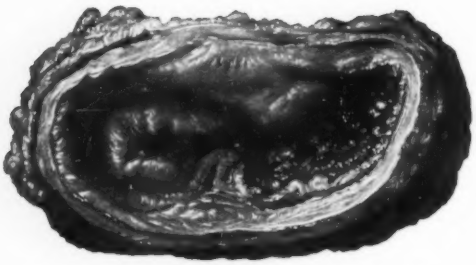

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FIG. 13.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting, with Extensive Necrosis (Gyn. Path. No. 7602).

Patient 40 years old; 3 children (age ?). Uterine bleeding and a foul discharge had been present for eight months, patient had been treated locally with electricity, twice a week, during the last four months. Pain, she had, was probably due to the pelvic inflammatory disease. General condition was fairly good, hæmoglobin 70 per cent.

Movements of the uterus were slightly restricted and the involvement of the left side of the vagina probably accounted for the apparent indurated parametrium of that side.

Vaginal portion of the cervix (natural size and never curetted), shows that the cervix has been converted into a craterous cavity lined by friable cancerous tissue, which has destroyed the greater portion of the vaginal portion of the cervix and has invaded the left side of the vagina.

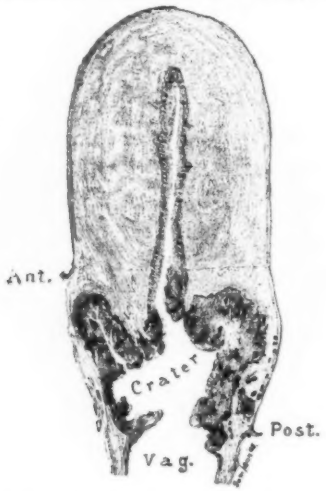

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FIG. 14.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 13.

The cavity was caused by the necrosis of the cancer and shows how the disease usually stops at the level of the internal os.

Parametrium of both sides were involved by a direct extension of the disease and a metastasis to a parametrial lymph node was found in the left side. Cancer was not found in the pelvic lymph nodes examined.

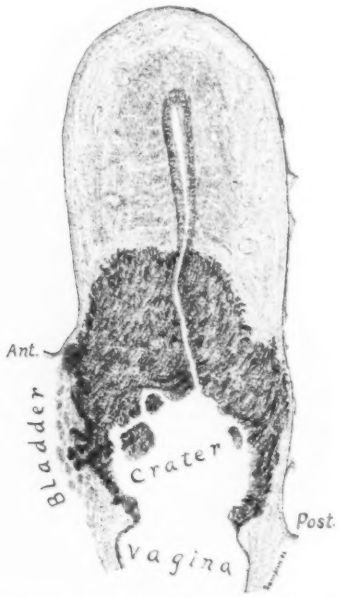

FIG. 15.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting; Extension with Involvement of the Bladder (Gyn. Path. No. 6715).

Patient 36 years old; 7 children (18-5 years). Uterine bleeding, alternating with a foul discharge, had been present for four months. Slight pain in the lower abdomen was probably due to adhesions from the pelvic inflammatory disease. General condition was fairly good.

Movements of the uterus were limited by the pelvic inflammatory disease and extension of the disease into the parametrium.

Stained sagittal section of the uterus demonstrates the invasion of the bladder muscle and the craterous cavity resulting from the necrosis of the cancer. The disease had invaded both parametria and had metastasized to the pelvic lymph nodes. The body of the uterus is beginning to be invaded by the growth.

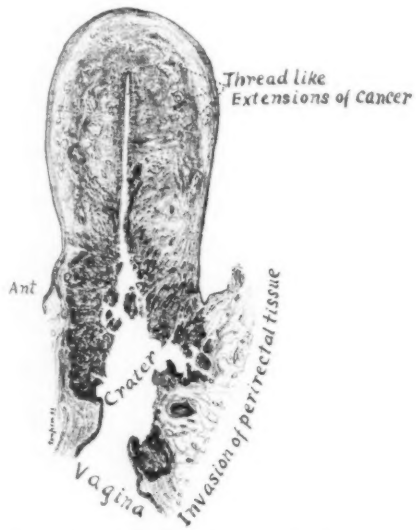

FIG. 16.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting; Extension with Obliteration of the Cul-de-sac and beginning Involvement of the Rectum (Gyn. Path. No. 7419).

Patient 37 years old; 6 children (14 years to 13 months). Bleeding, of ten months' duration, began three months after her last pregnancy. Condition was fairly good, hæmoglobin 73 per cent.

Movements of the uterus were restricted by the extension of the growth posteriorly and also by the apparent induration of the parametrium.

Stained sagittal section of the uterus shows the craterous cavity resulting from the necrosis of the growth, the extension of the disease into the body of the uterus as thread-like processes and the direct extension of the disease posteriorly obliterating the cul-de-sac and invading the tissue about the rectum.

The parametrium was involved by direct extension and cancer had metastasized to the pelvic lymph nodes.

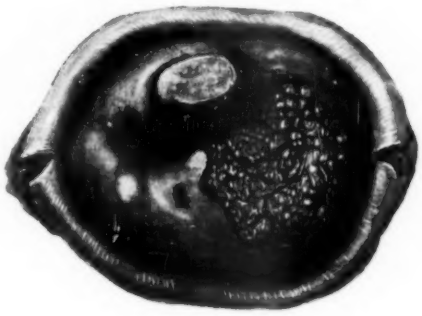

FIG. 17.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; both Inverting and Everting (Gyn. Path. No. 7467).

Patient 50 years old; 3 children (25-20 years); menopause one year ago. Bleeding had been present for three months, first noticed when straining at stool, severe hæmorrhages six weeks ago, and more or less constant offensive watery discharge, but no pain. General condition was good, hæmoglobin 74 per cent.

Movements of uterus were limited by pelvic adhesions, but the parametrium felt normal.

Vaginal portion of the cervix (natural size and not curetted), shows that the entire cervix is indurated and the outer portion of the posterior lip has become "ulcerated" and from the floor of the ulcer has arisen a cauliflower or everting growth. Another cauliflower growth is seen, about to "burst through" the center of the anterior lip.

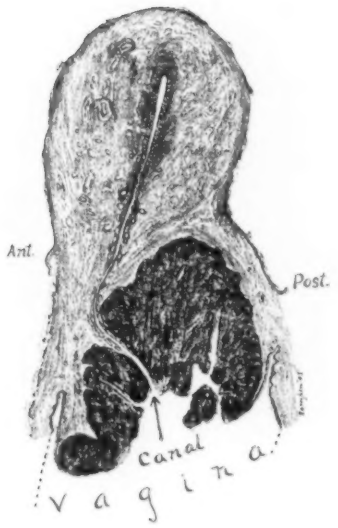

FIG. 18.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 17.

The growth is invading the cervical tissue *en masse* and in the posterior wall has reached the level of the internal cervical os. Notice how it grows through the cervical tissue and not along the cervical canal.

The adhesions on the surface of the uterus are shown. Cancer was not found in either the parametrium or pelvic lymph nodes removed.

FIG. 19.—Squamous Cell Carcinoma, Cervical Canal; Everting. Causing Occlusion of the Canal and Pyometra (Gyn Path. No. 7658).

Patient 63 years old; 7 children (youngest 26); menopause sixteen years ago. Bleeding for three months had been the only symptom. General condition was excellent, hæmoglobin 85 per cent.

Movements of the uterus were limited by pelvic adhesions from double pyosalpinx, probably secondary to pyometra. Parametrium on both sides was indurated.

Vaginal portion of the cervix (natural size and not curetted) has become indurated, retracted and puckered and protruding from the external os is a cauliflower or everting growth.

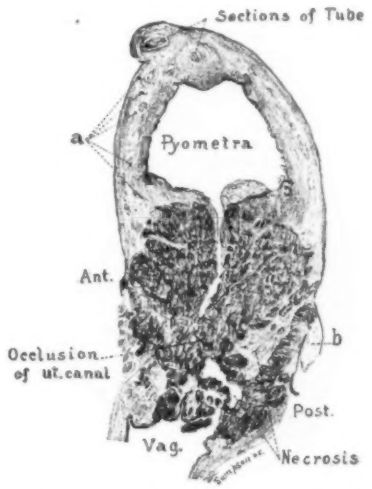

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FIG. 20.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 19.

The canal has been occluded by the growth, causing a pyometra. The fundus has become invaded by thread-like extensions of the growth (a) and the invasion of an adherent epiploical appendage of the sigmoid (b) is shown. The retracted shrunken and puckered vaginal portion of the cervix is also shown.

The parametrium on both sides was invaded by the growth and metastases to the pelvic lymph nodes were found.

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FIG. 21.—Squamous Cell Carcinoma, Cervical Canal; Inverting (Gyn. Path. No. 8153).

Patient 46 ? years old; 9 children (youngest 10 years). History very unsatisfactory, but symptoms apparently of very short duration. Diagnosis was made by curetting a small piece of tissue from within the external os. General condition was excellent.

Uterus was freely movable and parametrium on both sides was apparently normal.

Vaginal portion of the cervix (natural size, had been curetted) showed absence of vaginal epithelium about the external os, probably caused by the curette. The anterior lip was a little retracted about the external os and just within the canal could be seen friable cancerous tissue.

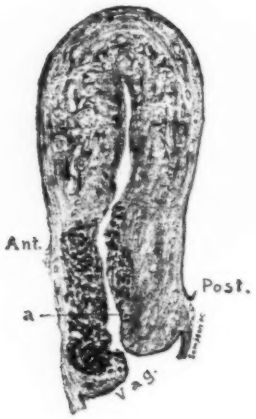

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FIG. 22.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 21.

The growth has started within the canal and has involved the latter as high as the internal os and is invading the cervical tissue on all sides in a diffuse manner. (a) represents the junction of the vaginal mucosa and the growth within the posterior lip.

Cancer was not found in the parametrium. The pelvic lymph nodes had not been removed.

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FIG. 23.—Squamous Cell Carcinoma, Cervical Canal; Inverting. A Later Stage than One Shown in Fig. 21 (Gyn. Path. No. 6074).

Patient 54 years old; 6 children (youngest age ?); menopause eight years ago. Bleeding had been present for eight months, constant but never profuse; no other symptoms. General condition was good, hæmoglobin 75 per cent.

Uterus was movable, parametrium of the right side was apparently normal, that of the left side felt slightly indurated.

Vaginal portion of the cervix (natural size—small piece removed from within the canal for diagnosis) shows very well the indurated, retracted, and puckered vaginal portion of the cervix caused by the invasion of the cervical tissues from above.

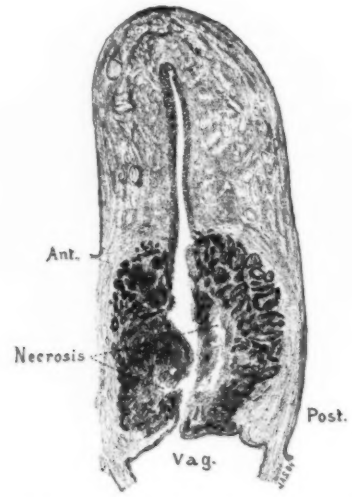

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FIG. 24.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 23.

The growth has started within the canal and has involved nearly the entire cervix extending above as high as the internal os. Metastases had occurred to the lymph nodes of both the parametrium and the sides of the pelvis.

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FIG. 25.—Squamous Cell Carcinoma, Cervical Canal; Inverting. A later stage than the one shown in Figs. 23 and 24 (Gyn. Path. No. 6860).

Patient 48 years old; 8 children (aged ?); still menstruating. Bleeding had been of eighteen months' duration, foul watery discharge of shorter duration, some pain possibly due to the adhesions from a previous pelvic inflammation. Uterine polyp, may have accounted for some of the bleeding. Condition was fairly good, hæmoglobin 80 per cent.

Movements of the uterus were restricted and parametria of both sides felt indurated.

Vaginal portion of the cervix (natural size and never curetted) shows very well how the growth within may be very extensive and yet the vaginal portion of the cervix may be but very little involved. Notice the shrunken, puckered, and retracted vaginal portion of the cervix caused by the necrosis of the growth.

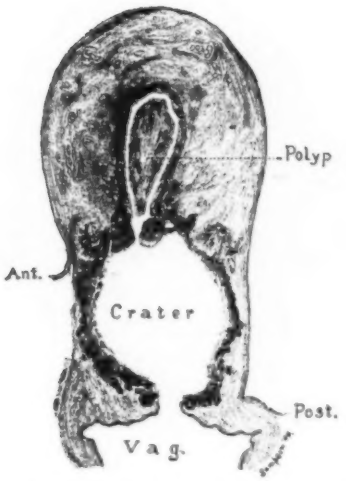

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FIG. 26.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 25.

The "craterous" cavity resulting from the necrosis of the growth is shown and the latter is beginning to invade the body of the uterus. A polyp is present in the fundus.

There was hypertrophy of the connective tissue of the parametrium, but the primary growth was apparently limited to the uterus. Metastases were found in the pelvic lymph nodes of both sides.

FIG. 27.—Squamous Cell Carcinoma, Cervical Canal; Inverting. An Extensive Growth of "Scirrhus" type (Gyn. Path. No. 7468).

Patient 37 year old; 7 children (15-2½ years). Bleeding had been the only symptom; of two years' duration, at first irregular but very profuse; constant the last three months. Patient was anæmic, hæmoglobin 55 per cent.

Parametrium was apparently indurated, growth had involved the deeper tissues of the vagina, all around the cervix.

Vaginal portion of the cervix (natural size, never curetted), shows that both lips present an "eroded" appearance with an irregular "fringe" of vaginal mucosa about the circumference. The eroded portion of the cervix appears "honey-combed" and the vagina about the cervix is indurated as a result of the invasion of its deeper tissues.

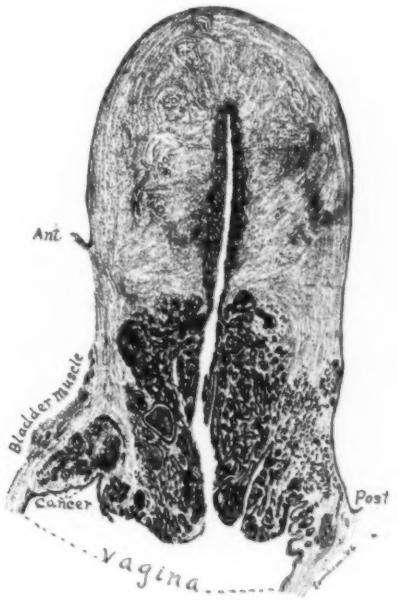

FIG. 28.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 27.

The growth is shown invading the deeper vaginal tissue, and the vaginal mucosa of the vaginal portion has sloughed off from the greater portion of both cervical lips. The disease does not extend above the internal os.

The growth had also extended in the parametrium of both sides, but cancer was not found in the pelvic lymph nodes removed.

FIG. 29.—Squamous Cell Carcinoma; Inverting; Origin ? but probably Vaginal Portion of Cervix (Gyn. Path. No. 7370).

Patient 35 years old; 2 children (ages?). A leucorrhœal discharge had been present for six months, bloody every time she had sexual intercourse or used a douche. Pain, for several years, was due to pelvic adhesions from previous inflammatory trouble. General condition was fair, hæmoglobin 75 per cent.

Uterus was adherent, parametrium on both sides indurated, and posterior vaginal wall involved.

Vaginal portion of the cervix (natural size, never curetted), shows that both lips present an "eroded" appearance, the posterior lip being much larger than the anterior, and on the outer right half of the latter a small area of mucosa is still present. The growth has involved the entire posterior vaginal wall, causing a large ulcer whose floor is composed of friable cancerous tissue.

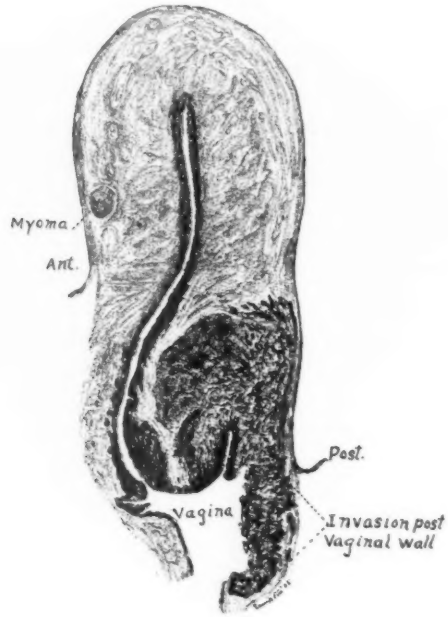

FIG. 30.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 29.

The growth is limited almost entirely to the deeper tissues of the posterior cervical wall and vagina. The cervical canal is involved only about the external os and for a short distance within, the anterior lip is compressed, and involved only about the external os.

Cancer was found in both the parametrium and pelvic lymph nodes.

FIG. 31.—Adenocarcinoma; Cervical Canal—Originally Everting (Gyn. Path. 6603).

Patient 37 years old; 4 children (21-15 years). Bleeding began seventeen months ago, and seven months ago a fungoid growth was removed from the cervix and there has not been any bleeding since, but for the last five months there has been severe pain in lower abdomen and back, requiring morphia. General condition was fairly good, hæmoglobin 60 per cent.

Uterus was movable, parametrium of each side felt normal.

Vaginal portion of the cervix (natural size and from which a fungoid growth had been removed seven months ago) shows that both cervical lips appear normal, but the external os is a little enlarged, edges ragged, and within can be seen and felt friable tissue.

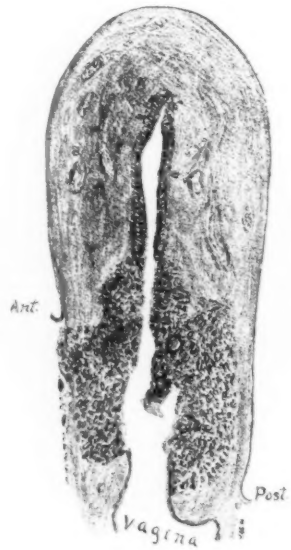

FIG. 32.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 31.

An adenomatous growth has invaded nearly the entire cervix about the external os and is gradually replacing the endometrium of the body of the uterus.

Cancer was present in both the parametrium and pelvic lymph nodes.

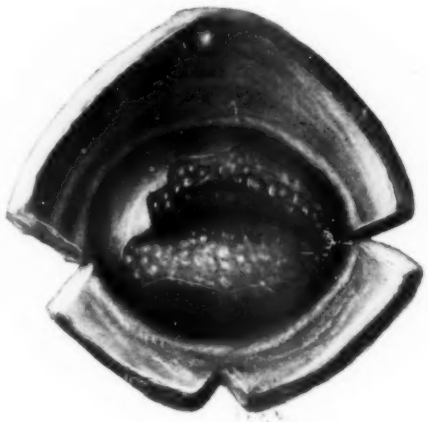

FIG. 33.—Adeno-carcinoma, Probably Starting in the Cervical Canal; Inverting (J. H. H., Path. No. 2377).

Patient 40 years old; 7 children (13-2 years). Bleeding for six months had been the only symptom. Local treatment before entering the hospital (length of time?). General condition was bad.

Uterus was movable, some induration of the left parametrium. Patient died from cerebral embolism, following acute endocarditis. Specimen was obtained at autopsy a few hours after death.

Vaginal portion of the cervix (natural size, local treatment, including curettage for sometime before patient came to hospital), shows that about one-third of the surface is covered by mucosa, while the rest presents an "eroded" appearance, the extreme left side and also the portion of the anterior lip about the external os being composed of friable tissue which bled on palpation. A small cancerous nodule was found in the anterior vaginal wall about 1.5 cm. from the cervix.

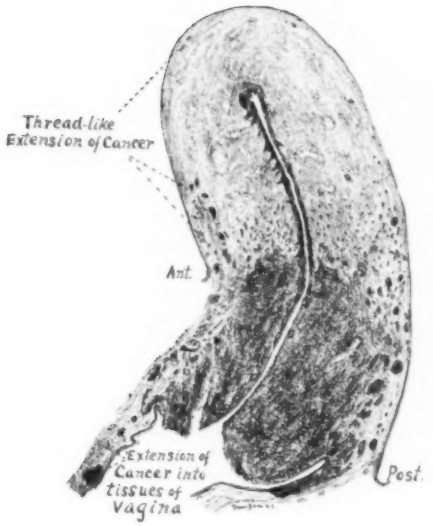

FIG. 34.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 33.

The growth apparently started from the deep cervical glands, the superficial cervical mucosa being for the most part intact. The growth has invaded the body of the uterus and the deep tissues of the vagina.

Cancer was found in the parametrium of both sides, liver, diaphragm, lungs and thoracic, abdominal and pelvic lymphatics.

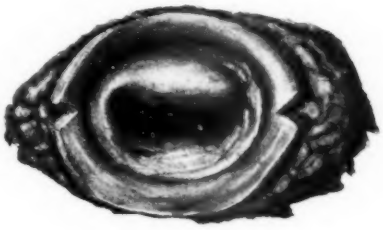

FIG. 35.—Adeno-carcinoma; Cervical Canal, with Possibly Squamous Cell Carcinoma of Vaginal Portion of Cervix (Gyn. Path. No. 8154).

Patient 62 years old; 4 children (41-35 years); menopause seventeen years ago. Constant bloody discharge had been present for seven months, and at times bearing-down pains in the uterus. Condition was fairly good.

Movements of the uterus were restricted by adhesions from previous pelvic inflammation. Parametrium on the left side felt indurated.

Vaginal portion of the cervix (natural size and never curetted) shows the shrunken, puckered, and retracted cervix, so characteristic of the advanced cases of cancer developing within the canal. Just within the external os, friable tissue which bled easily could be palpated.

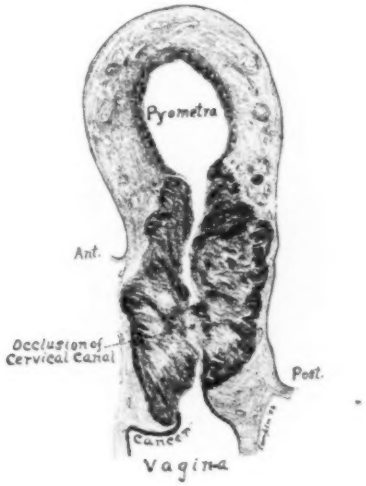

FIG. 36.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 35.

The growth has occluded the cervical canal causing pyometra. It is also beginning to invade the body of the uterus. The vaginal portion of the uterus is apparently covered by a thin layer of cancerous tissue of the squamous cell type which, to the naked eye, looks like the normal mucosa.

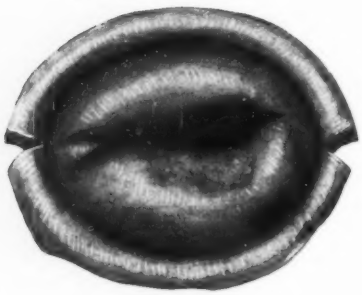

FIG. 37.—Adeno-carcinoma ?; Cervical Canal; Inverting. Very Malignant (Gyn. Path. No. 6763).

Patient 41 years old; 1 child (9 years). Only symptom was bleeding, of three weeks' duration. General condition was excellent, hæmoglobin 85 per cent.

Uterus was freely movable; apparently a very early growth.

Vaginal portion of the cervix (natural size, a small piece had been removed from within the external os for diagnosis) is apparently normal for a parous woman, except for a small nodule of tissue seen just within the external os and apparently arising from the anterior cervical wall.

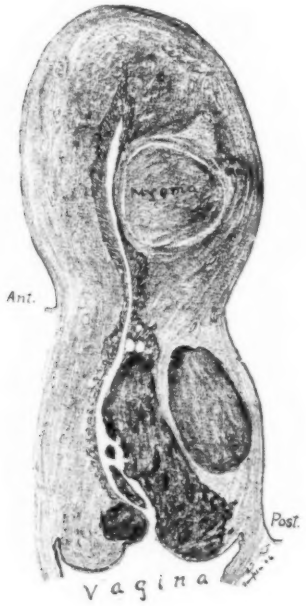

FIG. 38.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 37.

A growth has arisen from within the cervical canal, apparently an adenocarcinoma. It has spread over the posterior surface of the cervical canal and is invading the deeper tissues. The anterior surface of the canal is involved just within the external os; a second cancerous nodule or part of the primary growth is seen just posterior to the other. It was impossible to determine its exact relation to the first one. Cancer was not found in the parametrium. The growth recurred soon after operation.

the fifteen cases, there was a history of neglected uterine bleeding for six months or more, but in two cases with metastases to the pelvic lymph nodes this was of less than two months' duration. As the disease invades the cervical tissue, necrosis usually occurs with a resulting ulcer. Occasionally the tumor may increase greatly in size with but very little necrosis, but usually the one closely follows the other. As the cervical tissue becomes invaded by the growth necrosis usually occurs, later the cervical canal becomes surrounded, then invaded and the central core of the cervix may slough away, and thus convert the cervix into a crater lined with cancerous tissue.

In the seven cases of bleeding for six months or over, the cervix had been converted into a crater in four of the cases. While a long duration usually indicates an extensive growth it does not necessarily follow as shown in Fig. 9, nor does one of apparently short duration indicate an early one, see Fig. 11.

This type of growth is a very unfavorable one, usually soon invading the surrounding tissues and even metastasizing before the latter becomes involved. The symptoms may appear early or late, depending on how soon necrosis appears and its extent. We are unable to make a definite prognosis from the history of the case, or the results of clinical or pathological examinations unless it be that if metastases are present the prognosis is very unfavorable. A history of long duration may reveal an early growth, one of short duration an extensive one, and a small primary growth may give rise to metastases and an extensive one may still be local.

Squamous Cell Carcinoma—Cervical Canal.

This occurred in five instances, in four cases inverting and in one everting. In the latter case, pyometra was present. The inverting type of growth undergoes the same changes as the inverting type arising from the vaginal portion of the cervix. It, however, offers the additional clinical disadvantage that it is situated within the cervical canal and this renders its diagnosis by inspection or palpation more difficult. It is remarkable how far advanced the growth may be and yet the mucosa of the vaginal portion of the cervix may be intact or but little involved, as shown in the illustrations. There is one very important clinical feature to be emphasized and that is the induration, retraction, and puckering of the vaginal portion of the cervix caused by the growth invading it from above, analagous to a similar condition of the skin or nipple of the breast usually seen in cancer of that organ.

The Clinical Significance of Adeno-carcinoma of the Cervix.

There were but four instances of this type of growth, and all arose in the cervical canal. One was probably of the everting type but the everting part had been removed before I saw the patient. In all specimens the growth had extended beyond the uterus, and all four patients are dead. One died from cerebral embolism due to acute endocarditis, another died on the fifteenth day after hysterectomy, and the two others died from recurrences within a year and a half after hysterectomy. All four cases could not have been cured at the time of the operation. Bleeding as a symptom was present in these four cases; in one three weeks, in the three others six, seven, and seventeen months, respectively.

These four cases support the view that this is the most malignant form of uterine cancer.

CONCLUSIONS.

From a study of these cases, some of the types of cervical cancer may be seen and the changes they undergo as the disease progresses, and from this study we are able to understand the clinical manifestations of the disease. One very important feature must be emphasized and that is the importance of an early diagnosis, for the parametrium was involved in seventeen of the twenty-seven operable cases and the pelvic lymph nodes were involved in nine out of nineteen cases where they were removed and studied. In three of the nine cases in which the pelvic lymph nodes were involved, the parametrium was free, thus demonstrating that, in at least twenty of the twenty-seven cases, the growth had extended beyond the uterus.

One hopeful sign, however, was present and that is there was a history of neglected uterine bleeding for six months or more in over half of the cases. Put back the growth where it was six or even two months before the cases were operated upon and probably it would have been local in the majority of them. What we need is a *prophylaxis* of the incurable stage, and that can come only by the education of both physician and patient, the former first; and to him this contribution is offered.

STUDIES IN GENITO-URINARY SURGERY

THE JOHNS HOPKINS HOSPITAL REPORTS, Volumes XIII and XIV, will be issued in January, 1907. Volume XIII will consist of about 605 pages with 201 figures in the text, six plates and one colored chart.

Volume XIV will consist of about 632 pages, and have 97 figures in the text.

The price of each volume will be five dollars ($5.00), bound in paper, and five dollars and fifty cents ($5.50), bound in cloth.

Remittances and orders will now be received.

THE JOHNS HOPKINS PRESS, BALTIMORE, MD.

THE SURGERY OF BLOOD VESSELS, ETC.[1]

By Alescis Carrel.

Vascular surgery may be considered from the standpoint of the treatment of lesions of blood vessels proper, and from the standpoint of general therapeutics of tissues and organs. Treatment of lesions of the blood vessels, such as wounds, aneurisms, varices, etc,, constitutes classical vascular surgery, and its discussion therefore is unnecessary. Application of the vascular operations to general surgery is an almost unexplored field. I shall discuss to-night a few experiments of this character that Dr. Guthrie and I have performed since last August. I began these researches in 1901-1902 at the University of Lyons, and continued them last year with Dr. Guthrie at the University of Chicago, through the kindness of Dr. Stewart, who granted us the facilities of his laboratory.

I shall describe, first, *the operative methods*, second, their *experimental applications*, and third their *hypothetical applications to human therapeutics.*

A. Methods.

We use operations acting directly on blood vessels and operations acting indirectly on blood vessels through their nerves.

I. Operations acting directly on Blood Vessels are Five in Number: Partial Stenosis, Longitudinal Exclusion, Patching, Anastomoses, and Transplantations of Arteries and Veins.

In performing these operations certain general rules must be observed. It is known that failure in vascular surgery is mainly due to the formation of a thrombus. Pathological physiology of blood vessels shows that thrombosis may be caused by an inflammation of the endothelium, by a wound, even such as a slight crushing of the endothelium, by a lack of continuity of the intimal layers of the vessels, or by the presence of some foreign tissues or juices in the lumen of the vessel. Each detail of the technique (1), therefore, has been developed and adopted with the view of eliminating these sources of complication.

A rigid *asepsis* is absolutely essential for success. It seems that the degree of asepsis under which general surgical operations can successfully be performed may be insufficient for good results in vascular operations. Generally, it is considered that a wound is aseptic when it does not suppurate, and when healing occurs " per primam intentionem." But it should be remembered that this clinical asepsis is far from the ideal condition of absolute asepsis. Between absolute asepsis and infection, which is evidenced by the ordinary symptoms of inflammation, there are many intermediate degrees of attenuated infection. It is certain that every surgical wound, though clinically aseptic, is more or less infected. This infection may not be accompanied by the classical symptoms of inflammation; or if these phenomena are present, they may escape detection. The tissues unite " per primam intentionem," and from a clinical standpoint all the reparative processes occur as if the wound were really aseptic. But it is very probable that the more marked degree of these slight infections may be sufficient to cause thrombosis and that in order to obtain constant good results in blood vessel surgery the degree of asepsis must be higher than in general surgery.

The *dissection* of the vessel is not dangerous if the wall of the vessel is not crushed or roughly handled with metallic forceps or other hard instruments. Even the veins may be closely dissected and freely handled with the fingers without being injured, provided the wall be not hurt by a sharp instrument.

When *temporary hemostasis* is obtained by means of forceps or clamps, the endothelium is often wounded, and coagulation occurs at the injured point. It is necessary that these clamps be smooth-jawed and not too strong in the spring. We have abandoned completely this method of temporary hemostasis. The circulation is stopped by a narrow linen strip which is placed around the vessel, and then drawn tight and fixed by a serre-fine. This method does not injure the wall of the vessel and its application is almost as rapid and no more difficult than the application of ordinary forceps. This small detail is of very great importance for successful results.

After section of the vessel, the *external sheath is resected* or *removed* from the edges of the lumen. For if it get between the edges of the vessels, which is very liable to happen, and come in contact with the blood, it very quickly leads to the formation of a thrombus. Next the lumen of the vessel is carefully washed with isotonic sodium chloride solution (0.9 per cent) and as a rule coated with vaseline. The vessel can be handled with very delicate forceps, if care is taken to grasp only the extreme edge of the wall.

On large arteries it is possible to make the suture by interstitial stitches without injuring the endothelium. But it is impossible on veins and on medium-sized and small arteries. As a rule perforating stitches are used, which, of course, produce wounds through the endothelium. Consequently it is necessary to render these wounds as harmless as possible. By using very sharp, round needles (No. 15 or 16), only extremely small wounds are made. As the vessel wall is very elastic and as it is stretched when the needle punctures it, the result is that it contracts down and holds the thread firmly. The threads are sterilized in vaseline and are kept heavily coated with it while suturing. The vaseline is rubbed off in the holes and prevents the wounded tissues and the blood from coming into actual contact.

Great care is taken not to include fragments of the connective tissue layer in the line of suturing, and to obtain a smooth union and approximation of the endothelial coats.

[1] Read before the Johns Hopkins Hospital Medical Society, April 23, 1906.

When these general rules are observed, the following operations are practically always successful.

1. *Partial stenosis.*—It consists of diminishing the size of the lumen of a vessel by one or more perforating stitches. The vessel is flattened between the fingers and transfixed with a fine needle in such a manner that the lumen is reduced as much as desired. The ligature is then drawn through and the two ends tied about the portion it is desired to occlude. A small hemorrhage occurs along the thread when it is drawn through, but this stops when the thread is tied.

This operation has been performed on the aorta, the carotid artery, and the portal vein of dogs, with the view of diminishing the circulation in the peripheral portions of the vessels (as Dr. Halsted (2) has done by the use of silver bands around the vessel). It was used also to increase the pressure of the portal vein and force its blood through the kidney, the renal artery being anastomosed with the splenic vein. It will be of value in producing congestion of an organ by diminishing the caliber of the veins in cases where this condition is desired.

2. *Longitudinal exclusion.*—It consists in isolating from the blood current a portion of the vessel of some length. Without interrupting the circulation continuous mattress sutures are made in such a manner that a longitudinal segment of the vessel is closed. This operation has been performed on the aorta and on the carotid. It is somewhat analogous to the reconstruction of the aorta proposed by Matas (3).

3. *Patching.*—This consists in closing an opening made through the wall of a vessel by sewing in it a portion of the wall of another vessel. For instance, an opening is made through the anterior wall of the carotid artery. A flap of proper size is resected from the wall of the external jugular vein. The edges of the venous flap are sutured to the edges of the arterial opening, and the circulation is re-established. It is possible to use a flap of peritoneum instead of a flap of vein. Three months ago, a small portion of the abdominal aorta of a cat having been extirpated, the wound was closed by a flap of peritoneum. Immediately after the circulation was re-established, the pulsations of the femoral arteries were normal and have remained so to the present time. The primary aim of the patching was the reparation of a vascular lesion, but it was also a preliminary step in the development of a method of lateral implantation of very small vessels. For instance, the spermatic artery of a medium-sized dog (20 K.) is so small that direct anastomosis is not feasible; but by dissecting it as far as the aorta and cutting out a triangular aortic flap, in the center of which is the mouth of the spermatic artery, and then suturing this flap on to a proper opening of the femoral or carotid arteries of another dog, successful transplantation may be performed. By this method, it is possible to transplant the smallest vessels.

4. *The direct vascular anastomoses* are made by uniting the edges of the openings of the vessels by a continuous suture (4 and 1). The *termino-terminal, latero-terminal* and *latero-lateral varieties* have been successfully established by this method with little difficulty.

The *termino-terminal anastomosis* is probably the most valuable. The most important stage of the operation is the approximation of the ends of the vessels by three threads applied in three equidistant points of the circumference of the vessels. Traction on each thread transforms the circumference into a triangle. While the sides of the triangle are stretched a continuous suture is made along each of them. The end to end suturing of the carotid artery of a dog can be performed in four or five minutes.

In the *termino-lateral anastomosis*, the end of the smaller vessel is united to a triangular opening made through the wall of the larger one.

The *latero-lateral anastomosis* consists simply of uniting by continuous suture and two triangular or ellipsoidal openings made through the wall of the vessels. This variety is used in our new method of making Eck's fistula.

This technique has some important modifications in the *arterio-arterial, veno-venous and arterio-venous varieties* (5), but the general principle is the same.

The main complications are hemorrhage, stenosis, and thrombosis. Hemorrhage occurs sometimes in arteric-venous anastomosis immediately after the re-establishment of the circulation. It is easily controlled by one or two additional stitches. Stenosis is very seldom observed; it never occurs when the edges are properly approximated and stretched during the suturing. Thrombosis is produced by infection or some grave fault of technique. For instance, in a case of transplantation of the kidneys in a cat, paralysis of the posterior limbs occurred a few hours after the operation. Post-mortem examination showed a complete obliteration of the lower aortic anastomosis, due to a lack of suturing of one-third of the circumference of the artery. The external sheath only was sutured, and of course, coagulation of the blood occurred.

Such complications are exceptional, and practically always the results are good, even after a long time. Clinical and anatomical examinations made six months-and-a-half to nine months after the operation demonstrated that the circulation through the anastomoses was as active as on the day of the operation, and that the anastomoses were perfectly sound and covered with a glistening and apparently normal endothelium.

5. *The transplantations of arteries and veins* (6).—There are two kinds of transplantations of arteries and veins, uniterminal and biterminal.

The *uniterminal transplantation* consists in grafting one end of a divided vessel into another point of the circulatory apparatus (7). There are many varieties of this kind of transplantation according to the nature of the vessels and to the combinations of their ends. An artery can be transplanted on a vein or another artery. A vein can be transplanted on an artery or another vein. On the other hand, the central or the peripheral end of a vessel can be transplanted on the central or peripheral end of another vessel or on its lateral wall. I have not time, of course, to describe each one of these varieties.

The main result of the uniterminal transplantation is to change the nature of the circulating blood, and to modify its

pressure. For instance, when the peripheral end of the external jugular vein is anastomosed with the central end of the carotid artery, the vein becomes filled with red blood; its pressure is increased while the pressure of the artery is diminished. From an anatomical standpoint, the vessels adapt themselves very quickly to these modifications of blood pressure. When the normal pressure of the carotid artery is increased by directing all its blood into a closed venous system, like the inferior thyroid vein, the wall of this artery becomes thicker. After a few months there is a hypertrophy of the muscular coat, and of the intima, changes which are similar to the internal and medial varieties of arterio sclerosis in man (8). It shows that in some cases arterio-sclerosis may be produced by a mere increase of blood pressure without intervention of toxic or microbian irritations. When the pressure of an artery is diminished by anastomosis with a large venous system, as the superficial veins of the neck, its wall undergoes phenomena of adaptation and becomes weaker. There is hypotrophy of the elastic and muscular elements of the middle coat. We intend, after having produced a sclerosis of the carotid, to try to cure it in producing a constant lowering of the blood pressure by a proper anastomosis.

When a circulation of red blood is established through a vein (9), its wall reacts very quickly by thickening itself. This thickening is produced mainly by the increase of blood pressure. The degree of thickening of the wall depends on the degree of the increase of blood pressure. When the vein supports a high pressure but lower than the normal arterial blood pressure, its wall becomes considerably thicker, its lumen is dilated and the circulation even after nine months is extremely active. It seems that the process of reaction stops when the thickening has reached a certain degree. On the contrary, when the venous wall has to support the normal arterial pressure, the thickening is very great. It seems that the process of reaction does not stop and may ultimately lead to a complete obliteration of the vein. After six months and a half, there was little circulation through the peripheral branches of a thyroid vein, which was anastomosed end-to-end to the carotid artery. All the blood of the carotid artery had been forced into the thyroid veins, and under this pressure, the wall had reacted as evidenced by extensive sclerosis.

The biterminal transplantation consists of cutting out a segment of a vessel and of interposing this segment between the cut ends of another vessel. It is termed *incomplete* when the vascular segment is allowed to retain its collaterals and its normal relations with the surrounding tissues. For instance, the ends of a segment of the femoral vein are cut, and anastomosed to the corresponding cut ends of the femoral artery. It is termed *complete* when a venous segment is completely extirpated and interposed between the cut ends of another vessel. An arterial or venous segment extirpated from an animal may be transplanted on the same animal or another animal. For instance, a venous segment is resected from a dog and substituted for a portion of the carotid artery of the same dog. It is an autoplastic transplantation. Homoplastic transplantations have also been performed. For instance, a segment of the aorta or the vena cava is extirpated and interposed between the cut ends of the aorta or vena cava of another animal.

After transplantation the nutrition of the vascular wall is excellent, the cicatrization of the ends is quickly made, and the circulation is perfect. The interruption of the circulation, which lasts from 20 minutes to two hours, does not appear to interfere with the nutrition of the vascular wall, and by taking care to preserve the vessel in sodium chloride or other suitable solution, it seems probable that the circulation could be interrupted longer without danger. When venous or arterial segments are transplanted respectively on a vein or an artery, no apparent changes in their structure occur. But when a venous segment is transplanted on an artery, it rapidly undergoes very pronounced modifications. There is no dilatation of the lumen of the vein. On the contrary, the venous wall reacts against the arterial blood pressure and becomes thickened. Fourteen days after the operation the venous wall was found very much thicker than the wall of the artery (10). This thickening was due mainly to hyperproduction of connective tissue, and to hypertrophy of the muscular and elastic portions of the venous wall. We do not yet know whether this thickening progresses indefinitely and leads to stenosis or obliteration of the vessels. Five months after the operation a venous segment transplanted on the carotid artery exhibits the appearance of an arterial segment, pulsates as an artery, and its circulation is very active.

We may conclude that the vessels adapt themselves very quickly to the changes of pressure and function. This power of adaptation makes vascular transplantations one of the fundamental operations of experimental blood vessel surgery.

II. Operations acting on the Blood Vessels through their Nerves.

Three kinds of operations have been performed: (11) *temporary partial or complete denervation* of the kidney, *elongation* and *crushing* of the nerves of the thyroid gland.

Temporary denervation consists of cutting the nerves of an organ and of anastomosing immediately the main fibres. For instance, the kidney of an animal is completely denervated by closely dissecting the vessels. Both ends of the main nerve may be anastomosed by using a fine needle. In one case the peripheral end was united to the great abdomino-genital nerve, in order to change the innervation.

Elongation and *crushing* of nerves are such simple operations that they do not need to be described.

It is well known that section of their nerves produces vasodilatation of organs. The physiological effects of denervation are easily observed after replantation and transplantation of organs. Complete denervation is not necessary, for a partial denervation of the kidney may be followed by marked vasodilator phenomena. Elongation and crushing produce effects similar to those produced by section of the nerves. This method of producing an increase of the circulation of organs must be considered as crude and inexact, as excitatory fibres as well as vaso-constrictor and vaso-dilator fibres are cut

at the same time. On the other hand, section of nerves is always more or less harmful. In order to develop a better method, it would be necessary to exactly establish the topography of the different kind of nerves. This might enable us to cut only the vaso-constrictor nerves. The ideal operation would be to produce a permanent excitation of the vaso-dilator or vaso-constrictor, or even excitator nerves, according to the needs of the organ. This question is now being studied, but the results as yet warrant no conclusions.

B. Experimental Applications.

The experimental applications of these operations are very numerous. It was quite impossible to make an exhaustive investigation of this large field within a few months with such facilities as we had. I shall briefly describe some experiments performed with the view of observing *the effects of artificial modifications* of the circulation *in the limbs, the head,* and *the organs;* and secondly, the *preliminary researches on the question of the transplantation of organs.*

1. Artificial Modifications of the Circulation in the Limbs, the Head, and the Organs.

We tried to *modify the circulation of the posterior limb* by lateral anastomosis of the femoral artery and vein and the cross end-to-end anastomosis of the femoral artery and vein, and the aorta and vena cava. The lateral arterio-venous anastomosis was proposed in 1902 by san Martin y Satrustigui as a treatment of gangrene (12). He established a lateral anastomosis between the femoral artery and vein on goats, but obliteration occurred. He also performed this operation on two patients affected with gangrene of the lower limb. In one case the operation was entirely unsuccessful, in the other the gangrene stopped, but this was probably due to the fact that the affected portion was amputated at the time the anastomosis was performed. Afterwards, Jabouley (13) made the same operation on a patient suffering from gangrene produced by endarteritis. The operation was not successful and amputation became necessary. The idea of san Martin y Satrustigui was ingenious but his method and also that of Jaboulay was wrong, because after a lateral arterio-venous anastomosis the larger part of the arterial blood instead of going towards the capillaries goes back towards the heart through the central end of the vein. At the same time the arterial blood pressure is considerably lowered. We have shown by performing on a dog a lateral anastomosis between the femoral artery and vein, that three hours after the operation the valves are still competent and that no red blood flows through the veins towards the capillaries, but that it flows towards the heart (14).

On the contrary, by performing a cross end-to-end anastomosis of the femoral artery and vein, the circulation is quickly reversed (14 and 15). An acute experiment on a dog showed that three hours after a termino-terminal anastomosis of the central end of the femoral artery to the peripheral end of the femoral vein, the veins of the thigh, the leg, and the foot were filled with red blood, and that the dark blood returned toward the heart through the arteries. Complete reversal of the circulation in the limb is practically achieved four hours after the operation. A dog with a partial reversion of the circulation in the posterior limb was kept alive for several weeks and no trouble occurred. But this does not prove that a complete reversal is not harmful for the nutrition of the limb. It is probable for many reasons that this operation will not have practical applications in the treatment of gangrene. It may, however, be useful for some other purposes. For instance, a preliminary study was made of a method for directing a current of red blood through the venous apparatus of the epiphysis of a bone, in order to increase the rate of its development. But at the present time no conclusion can be drawn as to whether or not this operation can give positive results. While a partial reversal of the circulation in a limb may be of value, a more extensive operation, as the simultaneous reversal of the circulation in both posterior limbs, is very dangerous. If, for instance, the central end of the abdominal aorta is united to the peripheral end of the vena cava and the central end of the vena cava to the peripheral end of the aorta, the circulation is immediately reversed in the lower part of the abdomen and the upper part of the hind limbs, the valves stopping the blood from the lower portion of the latter for a time. By degrees, however, they give way, and at the same time the animal may present symptoms of a very abundant hemorrhage, even becoming comatose. If at this stage the head be lowered and the posterior limb elevated, it immediately regains consciousness and shows ambulatory movements of the fore limbs. Post-mortem examination of such a case shows an enormous congestion of the veins below the level of anastomoses, the animal dying apparently by collection of the red blood in the venous system.

Artificial modifications of the circulation of the head and neck are easily obtained, for the veins are practically without valves.

The *transformation of the superficial veins of the neck into arteries* has often been performed by anastomosing the carotid and the external jugular vein. After several months all the superficial veins of the anterior part of the neck are still filled principally with red blood. Six months-and-a-half after the operation their walls were found to be markedly thickened. The subcutaneous veins were similar to small arteries, and the thickness of the skin was increased.

We tried to increase the circulation of the brain by directing a strong current of red blood through the internal jugular vein, the peripheral end of this vein being anastomosed to the central end of the common carotid artery. After this operation no clinical troubles occur in the dog, a dog operated on five months ago is living in good health, but it might not be the same in man, as in the latter the internal jugular vein is more important than in the former. This idea of using the veins to conduct the red blood to the brain is not a new one. Jaboulay in 1902 expressed the opinion that an arterio-venous anastomosis might have a good result in case of insufficient circulation, as in softening of the brain. I do not think that this kind of lesion can be successfully treated, but it is not

absolutely improbable that a slow and progressive disease such as cerebro-sclerosis might be benefited by an operation modifying the circulation. But on account of the special conditions of the circulation of the brain, the substitution of veins for arteries to advantage when the latter are rendered useless by some pathological processes, is doubtful.

A few operations were performed with the view of *regulating the arterial circulation of the brain* in such a way as to diminish the blood pressure or to protect the brain against sudden increase of the blood pressure.

We attempted to suppress the arterial pulsations in the upper part of the carotid artery. For this purpose the length of the carotid artery was increased and its shape modified by interposing between its cut ends a long and curved segment of vein. From a theoretical point of view the systolic wave should be altered by the difference in elasticity of this thin and half circular venous tube. The tracings taken above and below the venous segment showed that this view was true, as regards the immediate results. But these results cannot be permanent as the wall of the vein rapidly becomes greatly thickened. However, owing to its semicircular shape, the venous segment may alter the circulation in a manner similar to that effected by the normal curvature of the vertebral and the upper portion of the carotid artery.

We endeavored also to diminish the pressure of the cerebral arteries in order to modify their structure. The central end of the external jugular vein was implanted on the wall of the common carotid artery. A large part of the arterial blood flowed into the vein with a strong thrill. A tracing taken from the central end of the carotid of the other side showed a lowering of the pressure when the blood was allowed to escape into the vein. Still another and more radical operation was performed. The peripheral end of the carotid was united to the central end of the jugular vein, in such a manner that the circulation of the carotids were reversed. The carotid then became similar to a vein, only it carried red blood toward the heart. This anastomosis probably produces a lowering of the cerebral blood pressure. A sudden increase of the arterial pressure would probably produce less effect on the cerebral circulation than normally, owing to the escape of arterial blood into the venous system. This operation may protect the vessels of the brain against great actual variations of the blood pressure. A dog thus operated on eight months ago is still living and in good health, and will enable us to study the anatomical modifications of the vessels. It is not entirely unreasonable to believe that operations of this character may sometime be used to hinder cerebral hemorrhage and perhaps to treat sclerosis of the arteries by establishing a lower pressure in the cerebral vessels and so producing a modification of their anatomical structure. This is, of course, a mere hypothesis, and further experiments may show that it is quite impossible.

The artificial modifications of the circulation in organs may be accomplished in a number of different ways. A few of these possible operations have been performed with the intention of changing the kind of blood circulating through a gland. We have tried mainly to increase the amount of red blood, or, in other words, to produce arterial hyperemia of the organ.

The substitution of the blood of the portal vein for the red blood of the renal artery was made with the view of investigating whether an organ can live with only a circulation of dark blood. The peripheral end of the renal artery was anastomosed to the splenic vein, and the pressure artificially increased in the portal vein by producing a stenosis near the liver. The dark blood flowed through the renal artery, the kidney, the renal vein and into the vena cava. In one case the kidney was examined through an incision fifteen days after the operation. The renal tissue was very pale and soft, and on cutting it a hemorrhage of dark blood occurred. There was no secretion of urine. Also it would be very easy to make the venous blood from one kidney flow through the other kidney by anastomosing the peripheral end of the vein of the first kidney to the peripheral end of the artery of the second kidney. We intend also to suppress the red circulation of an exophthalmic goiter of a dog, and to supply the gland exclusively with dark blood.

Increase of the red blood supply of an organ has been secured by the complete reversal of the circulation, the transplantation of a large vein on an artery, and by temporary denervation or elongation of the nerves. Complete reversal of the circulation produced an arterial hyperæmia owing to the fact that the veins are larger than the corresponding arteries. It was tried on the kidney and successfully performed on a normal thyroid gland. The result was a temporary enlargement of the gland with increase of the circulation. The nutrition apparently remained unaltered. Transplantation of one or two large veins of the thyroid gland into the carotid artery produces a strong arterial hyperæmia. This hyperæmia is temporary for the venous wall reacts against the arterial blood pressure and becomes much thickened, the lumen being decreased in size so that several months after the operation the red circulation through the vein is greatly diminished. But even a temporary arterial hyperæmia produces great anatomical modifications in a pathological gland. This operation was performed four times on dogs presenting parenchymatous goiters. Although no conclusion can be drawn from these observations, one of them deserves description. An old dog had two very large parenchymatous goiters, which in shape, size, and consistency were similar. He presented some general symptoms attributable to an insufficient secretion of the thyroid gland. He was extremely fat, and had lost the hair from the lumbar and a part of the dorsal regions of his skin. He slept nearly all the time, or stupidly sat in a corner of the room. The operation was performed on the inferior thyroid vein of the right goiter, the left one being observed as a control. The vein became as large as the common carotid and exhibited the signs of having a strong arterial circulation. After a few days the right goiter began to decrease in size and became harder in consistency. At the same time the animal lost his excess of fat, hair grew rapidly on the bald spots, and he became very lively and pugnacious. Six months and a

half after the operation he was etherized and the goiter examined and extirpated. Profound modifications had occurred in the size and the consistency of the right goiter. It presented an appearance quite different from that of the left goiter. Its upper end, however, in which the circulation had not been modified showed a structure similar to that of the left side. Histological examination showed that the thyroid vesicles were very numerous, and the colloid substance abundant in the right gland, while very few were present in the left one. This shows that the increase of the red blood supply of a gland may perhaps produce modifications in its metabolism.

The circulation was increased in several cases by acting on the vaso motor nerves.

The operations of complete denervation, elongation and destruction of the nerves were performed on the normal thyroid gland. The results of these operations were a slight increase of the size of the organ and temporary exaggeration of the circulation. After a short time the gland regains its normal size. Temporary denervation was performed on the kidney. It produces at first the well-known effects of vaso dilatation and increase of the quantity of urine.

It is evident that there are other ways of modifying the circulation of an organ, and we have experiments planned along these lines. For example, the arterial flow may be diminished by section of the vasodilator nerves or permanent excitation of the vaso constrictors. If this operation were possible it would enable us to render less active the metabolism of a gland. On the other hand, it is easy to produce a venous hyperæmia by reducing the caliber of the veins. The experiments of Bier showed that venous hyperæmia gives excellent results in the treatment of diseases of the limbs. It would perhaps be true also for diseases of organs, and we intend to experiment along this line. These considerations show that the field of artificial modifications of the circulation is a large one and that a great many experiments must be made in order to determine if such operations may be of practical value.

II. Replantation and Transplantation of Organs and Limbs.

The *replantation* consists of extirpating an organ or a limb with its vessels, of putting it back into place and of re-establishing the circulation by anastomoses of its vessels. Hoepfner experimented with the replantation of limbs (16). We have replanted the thyroid gland (17), the kidney, the leg and the thigh (18) (19).

The extirpation and replantation of the thyroid gland with reversal of the circulation was successfully performed. The right thyroid gland having been dissected, all its vessels were ligated, except the superior thyroid artery and vein, which were cut near the carotid artery and the internal jugular vein. The gland was then extirpated and put in a glass of isotonic sodium chloride solution. After a few minutes, the thyroid gland was placed in the wound in the neck, and the peripheral end of the thyroid artery was united to the central end of the thyroid vein, and the peripheral end of the thyroid vein to the central end of the thyroid artery. The circulation was re-established about half an hour after the extirpation. The circulation through the gland was in a direction reverse to the normal. The red blood entered through the thyroid vein, and the dark blood flowed from the gland to the jugular vein through the thyroid artery. The hue of the gland was normal, and the circulation very active. Eleven days after the operation the wound was opened and the anterior portion of the gland directly observed. The gland was somewhat enlarged, but its hue and consistency were normal. Forty-seven days after the operation, the replanted gland appeared to be practically normal, being only slightly enlarged. Its systolic expansion was easily detected. Eight months after the operation the gland appears to be normal in size and consistency. It was at first superficially located, but it is now much deeper, being about in its normal situation.

The replantation of the kidney was also performed. The right kidney was extirpated, and carefully washed in salt solution. Then it was replaced in the abdominal cavity and the vessels anastomosed. Immediately after re-establishment of the circulation the kidney became uniformly red and clear urine began to flow from the ureter. The ureter was then anastomosed, and the kidney fixed in its normal place. Unfortunately an infection occurred, which resulted in obliteration of the anastomoses and the complete absorption of the organ.

The replantation of the leg was performed on a medium-sized dog. As the vessels were very small the anastomoses produced a stenosis and the circulation was not satisfactory.

On the contrary, the replantation of the thigh always gave an excellent re-estalishment of the circulation. This is an example of this replantation. Through a longitudinal incision the vessels of the thigh were exposed and cut above the point of Scarpa's triangle. The skin was circularly severed and the thigh completely amputated above the junction of its lower and middle third. After a few minutes the limb was replanted. The ends of the bone, the muscles, the vessels and the sciatic nerve were united. The circulation was re-established after having been interrupted for one and one quarter hours. The pulsations of the popliteal and "saphenous" arteries were normal. The dark blood circulated very actively through the femoral and saphenous veins. Red blood flowed from the small arteries of the peripheral part of the cut limb. The skin was sutured and a plaster dressing applied to the limb and trunk. After the operation the general and local conditions of the animal remained very satisfactory. It drank and ate normally and walked on its three sound limbs. The skin of the replanted foot remained normal, but its hue was redder and its temperature higher than that of the normal foot. The anterior part of the foot soon became moderately swollen. Seven days after the operation the dressing was partially removed. The limb presented neither œdema nor trophic troubles. The œdema of the anterior part of the foot was doubtless due to pressure by the lower edge of the bandage, as the swelling completely disappeared within a few hours after correcting the fault of the dressing. The skin was normal and the wound had united "per primam intentionem" without evidence of inflammation. The temperature of the skin was

higher below than above the line of suturing. Eight days after the operation the foot appeared normal in size, all œdema having disappeared. On the tenth day, during the afternoon the temperature of the replanted foot became lower, *i. e.*, similar to that of the normal foot. The dressing was then removed. It was found that, owing to a slipping of the plaster bandage, some urine had got into the cotton dressing and caused infection of the upper part of the longitudinal incision. A small subcutaneous abscess had developed along the vessels. The general conditions of the animal were excellent, and the nutrition of the limb satisfactory. As the arterial pulsations were much weakened and as it was considered important to accurately determine the cause of this change, the animal was etherized and the vessels examined through cutaneous incisions, after which the animal was killed.

This dissection "in vivo" gave the following results: The point of the vascular anastomoses was surrounded by the small subcutaneous abscess. The venous anastomosis was good. The arterial anastomosis was partially occluded by a small clot. All the other portions of the vessels appeared perfectly normal. The circulation through the limb was yet satisfactory, as the obliteration of the anastomosis was not complete. The union of the skin, the muscles and the sciatic nerve was normal. The process of consolidation of the bone was beginning. It is probable, but not certain, that if the animal had been allowed to live, the arterial stenosis would have gradually increased and that in the end the circulation would have been interrupted. Then, no doubt, gangrene of the limb would have occurred, which result would have been due primarily to the secondary infection of the skin. This shows that in such experiments asepsis must be rigidly observed, not only during the operation but during all the post-operative period.

It is permitted to conclude that: (1) The circulation of a replanted limb, re-established an hour and a quarter after interruption, by end-to-end anastomosis of the femoral artery and vein, is normal, as judged by the metabolism of the limb. (2) No trophic trouble occurs (at least during ten days). (3) Healing of the severed tissues appears to be as rapid and complete as after an ordinary surgical wound.

The *transplantation of organs* consists of extirpating an organ with its vessels and grafting the latter onto the circulatory apparatus of the same animal or another animal. This operation may of course be autoplastic, homoplastic, or heteroplastic.

In 1902 I made the transplantation of the thyroid gland with its vessels (20), but it was not possible to observe physiological results, owing to the bad aseptic and technical conditions of the operation. Ullmann (21) made the first transplantation of the kidney by using the method of Payr (22). I was then ignorant of his experiments, and at about the same time (1901-1902) my investigations led me to the same experiments. In 1903 and 1904 similar experiments were made by Carl Beck of Chicago, Höpfner (23), Exner and Costello. In 1905 Floresco (24) continued these experiments and succeeded in transplanting the kidney into the lumbar region. In 1905 Guthrie and I performed the auto and homoplastic transplantations of the kidneys, the supra renal glands, the intestine, the heart, the lungs, the thigh, the ovary, and the heteroplastic transplantation of all the subdiaphragmatic portion of the body.

We use two methods of transplanting organs, *transplantation simple* and *transplantation en masse*.

The *transplantation simple* is the method mainly used. It consists of dissecting out the organ and its vessels and of anastomosing the latter to suitable vessels of the same or another animal. This technique has several drawbacks for the nerves and their sympathetic ganglia are cut off and the veins are unduly exposed to injury. The slightest fault of technique decreasing the caliber of the vessels may dangerously interfere with the circulation to the organ. Besides, it is absolutely impossible to perform the transplantation of organs like the testicle or the ovary on ordinary laboratory animals. For these and other reasons, we looked for a better method. This led to the development of the technique of *transplantation en masse* which consists of extirpating the organs together with its surrounding connective tissues, its nerves and ganglia, and its vessels with the corresponding segments of the large vessels from which they originate. This technique does not preclude injury of the nerves or their ganglia. Also a slight fault of technique in anastomosing large vessels is relatively of little importance. By this method transplantation of the testicle, ovary, suprarenal glands, et cetera, is rendered possible. We employed both methods according to the requirements, in the study of transplantation of organs.

Transplantation of the ovary (25) was performed as follows: The abdomen of a cat A being open, a large peritoneal flap, extending from the right ovary to the portion of the aorta corresponding to the mouth of the ovarian artery, is cut. The Fallopian tube is severed near its fimbriated extremity. The posterior surface of the peritoneal flap is carefully separated from all the posterior tissues excepting the ovarian vessels, which are permitted to retain their connection with it. Then the segments of the aorta and vena cava, from which the ovarian vessels originate, are extirpated. The specimen consisting of the ovary and a part of the Fallopian tube united to the segments of the aorta and vena cava by a peritoneal band and the ovarian vessels, is then placed in a glass of isotonic sodium chloride solution.

The abdomen of another cat (cat B) is then opened by performing a right, half-circular, transversal laparotomy. The right ovary and the external part of the Fallopian tube are resected. The aorta and vena cava are cut at the point of the mouth of the ovarian vessels. The anatomical specimen taken from cat A is removed from the salt solution and put into the abdominal cavity of cat B. The segments of the aorta and vena cava of cat A are interposed between the cut ends of the aorta and vena cava of the cat B. The peritoneal flap is attached to the posterior abdominal wall in such a manner that the transplanted ovary takes the place

of the normal ovary. The circulation through the aorta and vena cava is re-established. The red blood traverses the ovarian artery, the ovary becomes red, and the dark circulation is slowly established through the venous plexus and the ovarian vein. After a few minutes the circulation appears similar to that of the normal ovary. The end of the transplanted Fallopian tube is united to the end of the normal one. At last the suture of the abdominal wall is performed.

This operation is not very dangerous, for the animals a few hours after recovering from their anæsthesia appear to be in normal condition. Our experiments were performed on ordinary vagrant animals of uncertain breeds. They are only instructive, therefore, from a technical point of view. We intend to very soon perform a series of similar operations on pure breed animals, preferably dogs or pigs, with a view of studying the problem of transmission of characters and related problems.

The same procedure may be used for the transplantation of the testicle, and it would be better to use the method of patching instead of the biterminal transplantation. This transplantation of the ovary or testicle may be used for the study of the internal secretions by the multiplication of organs, for instance putting several testicles on the same animal or a large testicle on a small dog.

In the transplantation of the thyroid gland we used the simple method of transplantation. It might be useful to employ the method of transplantation *en masse* or by patching.

The *transplantation of a loop of intestine* into the neck was made as a preliminary study of the substitution of such a tube for the œsophagus. A segment of intestine was resected with its mesentery and vessels. The loop of intestine was put into the neck and its vessels implanted on the wall of the jugular vein and of the carotid artery. Soon after, the circulation was re-established the intestine assumed its normal hue. There appeared to be no vaso-dilatation, and twenty minutes later peristaltic movements were observed. They were spontaneous and easily exaggerated by mechanical excitation. The appearance of the bowel was entirely normal. Then its ends were sutured to the skin, and the wound closed. Unfortunately a phlegmon of the neck developed the following day, and it was necessary to extirpate the loop of intestine.

The *heart was* transplanted in several different ways. This is an example (26): The heart of a small dog was extirpated and transplanted into the neck of a larger one by anastomosing the cut ends of the jugular vein and the carotid artery to the aorta, the pulmonary artery, one of the venæ cavæ and a pulmonary vein. The circulation was re-established through the heart, about an hour and 15 minutes after the cessation of the beat; 20 minutes after the re-establishment of the circulation, the blood was actively circulating through the coronary system. An opening made through the wall of a small branch of the coronary vein led to an abundant hemorrhage of dark blood. Strong fibrillar contraction soon occurred. Afterward contractions of the auricles appeared, and, about an hour after the operation, effective contractions of the ventricles began. The transplanted heart beat at the rate of 88 per minute, while the rate of the normal heart was 100 per minute. A little later, tracings were taken. Owing to the fact that the operation was made without aseptic technic, coagulation occurred in the cavities of the heart after about two hours, and the experiment was interrupted.

We attempted also to make the *transplantation of the lungs together with the heart.* Both lungs, the heart, the aorta, and vena cava of a cat one week old were extirpated and put into the neck of a large adult cat. The aorta was anastomosed to the peripheral end of the carotid, and the vena cava to the peripheral end of the jugular vein. The coronary circulation was immediately re-established and the auricles began to beat. The lungs became red and after a few minutes effective pulsations of the ventricles appeared. But the lungs soon became œdematous, and distention of the right part of the heart occurred. This accident seems difficult of prevention. A phlegmon of the neck terminated this observation two days later.

The transplantation of the *suprarenal glands* was performed at the same time as the transplantation of the kidneys. From a macroscopical standpoint, it seems to be successful, but histological examination has not yet been made.

We performed the *autoplastic and homoplastic transplantation of one or both kidneys.* The kidney of a small-sized dog was extirpated and transplanted into the neck (27). The renal artery was united to the carotid artery, the renal vein to the external jugular vein and the ureter to the œsophagus. Three days after the operation the neck and the abdomen were opened, in order to study the functions of the transplanted kidney and to compare them with the functions of the normal kidney. The transplanted kidney was found adherent to the muscles, and dissection was necessary to free it. In size it was larger than the normal kidney. Its hue was darker. To the touch the consistency of its tissue was normal, and the pulsations of its artery were as strong as the pulsations of the artery of the normal kidney. The circulation in the transplanted kidney was slightly greater than in the normal kidney, as detected by the touch, copiousness of hemorrhage from incision in cortex, and pulse-tracings. The secretion of urine by the transplanted kidney was about five times more rapid than by the normal one. The intravenous injection of sodium chloride solution caused no change in the rate of secretion in the normal, but markedly increased the rate of the secretion in the transplanted organ. The composition of urine secreted by the transplanted kidney differed somewhat from that secreted by the normal one. The constituents were similar, but the chlorides appeared to be more abundant in the urine from the transplanted kidney, while the organic sulphates, pigments and urea were more abundant in the urine from the normal organ.

The autoplastic transplantation of the left kidney on the right side, after extirpation of the right kidney has been performed once. But infection immediately occurred producing

peritonitis, obliteration of the vessels, uremia, and death forty hours after the operation.

The homoplastic transplantation *en masse* was performed as follows (28): Both kidneys and the upper part of the ureters, together with their vessels, nerves, nervous ganglia, the surrounding connective tissue, the suprarenal glands, the peritoneum and the corresponding segments of the aorta and vena cava were removed. The mass was then placed in a vessel of isotonic sodium chloride solution. The aorta and vena cava of another animal were cut a little above the mouth of the ovarian vessels. The kidneys of the first animal were then removed from the salt solution and put into the abdominal cavity of the second, and the segments of the aorta and vena cava were interposed, by biterminal transplantation, between the cut ends of the aorta and vena cava. The circulation was re-established, after having been interrupted for one hour and a half. The kidneys immediately became red and turgid, as after a simple transplantation, but about half an hour later the state of the circulation became normal, so that no difference could be detected between the transplanted and the normal kidneys. Clear urine flowed abundantly from the transplanted ureters, which were united to the normal ones.

Both normal kidneys were dissected free and extirpated. The operation was completed by suturing the abdominal wall and applying the dressing. Two hours after the operation the animal walked about her cage. In the afternoon she drank and urinated copiously. The following day and subsequently, up to the eighth day, her diet consisted largely of meat, which she took hungrily. In general her condition was normal. During this period the urine remained clear, showing no evidence of containing blood. The total amount appeared to be somewhat increased. On the seventh and eighth days several samples were collected and analyzed, the results of which showed a slight variation in composition, but entirely within normal limits. The only abnormal constituent detected was coagulable proteid, the largest amount present in any of the samples being less than 0.25 per cent.

On the ninth day she began vomiting. A diagnosis of stenosis of the bowels by adhesions was made. On the tenth day the urine was analyzed and its composition was practically the same as before. As the animal was almost continuously vomiting, she was etherized and a laparotomy performed. We found localized peritonitis on the right side of the abdomen, with kinking of several loops of intestines, the mass being very strongly bound down by adhesions. The circulation of both kidneys was found to be perfect. There was an enormous hydronephrosis on one side.

We attempted to study the results of *heteroplastic transplantations of organs* from one species to another, but the experiments were unsuccessful and before making other attempts we intend to try to immunize the organs of an animal against the serum and organ extracts of another animal. On account of cytolysins it seems improbable that indiscriminate heteroplastic transplantation can be successfully performed. The transplanted organ must be prepared to support the serum of the animal on which it is to be grafted. We do not yet know if such immunization is possible.

C. Clinical Applications.

As yet it would be improper to draw definite conclusions from these experiments, for they are too incomplete. Therefore I would like to omit this part of the subject. But as immediate continuation of this work is doubtful, I shall briefly speak of its possible relations, first to the actual surgery of blood-vessels (26), and secondly to the surgery of organs and limbs.

I am very far from affirming that our plastic operations on blood vessels will on man give as good results as we have obtained on cats and dogs. Successful experiments on such animals do not warrant the drawing of definite conclusions as to their adaptability to man. The conditions as regards the vessels and the blood are different. The results would be doubtful if the operations were made on atheromatous arteries, sclerotic veins, or tissues of diathesic patients.

Nevertheless the use of our improved technic may be of value in all the actual operations on blood vessels (29). Thrombosis following the operations on blood vessels are due often to methods which do not properly meet the conditions for the continuation of the physiological processes. Therefore the results of the present blood-vessel surgery will be enhanced by the use of our methods of temporary hemostasis, of handling the vessels, of washing them with isotonic sodium chloride solution, of impregnating the threads and coating the vascular wall with vaseline, of exactly approximately the internal layers without invagination, and of suturing with very fine needles while the wall is somewhat stretched.

Some of the plastic operations may lead to the establishing of new therapeutic methods. For instance, the ideal treatment of large wounds of arteries and of aneurisms would be the extirpation of the diseased portion and the immediate re-establishment of the circulation (30). Hitherto, in exceptional cases the continuity of the artery has been re-established by end to end suturing. This is generally impossible on account of the gap between the cut ends of the vessel. But the continuity of the vessel would very easily be re-established by the biterminal transplantations of a vein or of an artery. After having extirpated an aneurism, it is possible to interpose between the cut ends of the artery a segment of the neighboring vein, or of some other vein, the saphenous or the external jugular for instance. If heterotransplantation prove successful, it may be possible to interpose between the cut ends of the vessel a segment of a vessel of a lower animal, *e. g.*, hog. This would annul the risk of gangrene following the extirpation of aneurisms. The other applications of these methods to the vascular surgery are so simple that they do not need description.

I shall briefly sketch their hypothetical applications to general therapeutics.

It is probable that the present surgery of organs is yet in its infancy. It consists mainly of section or of extirpation.

For example, when a kidney is inflamed a nephrotomy is performed. If the lesions are more serious, it is resected. When other organs less essential to life are diseased often they are extirpated without thought as to their physiological functions. It is not unreasonable to believe that, instead of cutting and extirpating a diseased organ, it may be possible to influence favorably its nutrition by operating on its vessels or nerves. On the other hand, when the extirpation of an organ is necessary the ideal treatment would be the immediate transplantation of a sound organ to take its place. Let us examine briefly these two hypotheses.

I. The nutrition and the functions of organs and tissues depend on their circulation and their excitator nerves. An increase of the circulation modifies probably the formative and productive power of tissues. It is reasonable to suppose that by increasing the metabolism activity of a diseased organ, it may be strengthened and enabled to overcome or to limit the morbid processes. We obtained an increase of the red circulation of the skin or of organs by acting on the blood vessels directly or through their vaso-motor nerves. The transplantation of a large vein into an artery produces a strong arterial hyperemia which seems entirely without harmful influence. Unfortunately we had no opportunity to use this method on organs presenting chronic or acute inflammation. It was applied only to benign growths of the thyroid gland, in which case it rapidly alters the anatomical structure, and appears to increase the glandular activity. If subsequent experiments demonstrate the constancy of these results, it should be possible with slight technical modification to use this method on man. Operations acting on the vaso-motor nerves alone are also able to cause an increase of the red circulation. Temporary denervation of organs, or stretching or crushing of their nerves is easier to perform than the operations on blood vessels, but may be more dangerous, at least for certain organs. These operations which consist in the simultaneous cutting of the vaso-motor and excitator nerves are of course very imperfect. Nevertheless they produce strong arterial hyperemia, and, on some organs, like the thyroid gland and the ovary, are probably harmless. It is known that section of all the nerves of the thyroid gland is followed by a temporary vaso-dilatation and that it does not produce any histological modifications of the cells. Our own experiments demonstrate that eight months after the extirpation and replantation, the thyroid gland is apparently normal in size, consistency and circulation. I have examined microscopically the section of an ovary of a chicken about fourteen months after it was transplanted by Guthrie. Its histological appearance was absolutely normal. Also it is known that the functions of a transplanted ovary may be completely re-established. For these many reasons we consider the denervation of the thyroid gland and the ovary as not dangerous. As regards the ovary, it would probably be better, from a physiological standpoint, to make the denervation rather than the resection of the organ, in a case of chronic inflammation.

In case of disease of the kidney, Bright's disease, for instance, the question is more complicated and cannot be settled at the present time. It is certain that complete denervation is harmful. However, the physiological experiments of De Vecchi showed that rabbits will survive after cutting all the nerves of both kidneys, though degenerative changes of the cells of the tubules were observed by him a few days after the operation. On the other hand, the urine of a transplanted kidney was almost normal ten days after the operation, and the animal did not present symptoms of uremia. For these reasons, I believe that the temporary denervation of the kidney is not very dangerous, but that it should not be used on man, at the present time. Partial denervation would be less dangerous. In a case of Bright's disease, in which medical treatment had failed, my friend Dr. Carl Beck, of Chicago, partially denervated one of the kidneys. Before the operation the amount of urine for 24 hours was 180 cc., and the urea less than 1 gm. for 100 cc. After the operation the amount of urine and urea became about 550 cc. and 15 g. respectively. Fifteen days after the operation the amount of urine was above 1000 cc. and the urea normal.

No conclusions, of course, must be drawn from this single observation, and, even if temporary denervation may yield successful results, we shall attempt to find some other operations producing vaso-dilatation of the organ without cutting of the nerves.

II. Clinical applications of the transplantations of organs are so obvious that they do not need to be described. If I were a veterinary surgeon and had to treat a myxœdematous dog, I would not hesitate to transplant into its neck a thyroid gland from another dog. In a case of a dog presenting Bright's disease, it would be a rational procedure to substitute for one of his kidneys a sound kidney extirpated from some normal dog. This operation would probably give good results, if performed on large-sized dogs and in a proper operating room. But the question of the transplantation of organs on man is difficult and very far from settled. In the first place, it is necessary to be sure that a transplanted organ may live in good condition after a very long time. This will be established only when a dog bearing the thigh or kidneys of another dog will have been kept in perfect health for years. Secondly, the difficulty of finding organs suitable for transplantation on man must be met. As regards the limbs, in which the tissues remain viable for a long time after interruption of the circulation it would be possible to use, immediately after death, the cadaver of an executed criminal or of a man killed by accident. It is not unreasonable to believe that some transplantations, as, for instance, the transplantation of the arm a little above the elbow, may be successfully performed if an adequate technique is used. As regards the kidneys, the thyroid and the glands in which the endothelium is easily injured by a short interruption of the circulation, the problem is more complex. For, if a limb can be separated from the body for several hours without great damage to its tissues, the same is not the case with a kidney. Then it would be extremely difficult to have an organ to transplant in good condition. In some exceptional cases it

would be possible perhaps to use the kidneys of a man killed by accident. Also the organs of the anthropoid apes are perhaps able to tolerate human plasma. But nothing precise is known in that respect. Besides, anthropoid apes are very expensive, and difficult to handle. Their use would propably be impracticable. The ideal method would be to transplant on man organs of animals easy to secure and to operate on, such as hogs, for instance. But it would in all probability be necessary to immunize organs of the hog against the human serum. The future of transplantation of organs for therapeutic purposes depends on the feasibility of heterotransplantation. Researches must be directed along this line, but as yet we have not been able to do more than perform a few preliminary experiments.

I must apologize for presenting such an important subject as this portion of the surgery of the blood vessels is, in a so superficial manner. The incompleteness of the experimental work is due, not so much to the difficulty of the experiments themselves as to the unsuitable surroundings in which they have been made. A great many other operations must be performed. Their results will indicate whether or not these researches may, in their limited field, contribute to the progress of the medical sciences.

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THE BLOOD OF NORMAL YOUNG ADULTS.

By CHARLES PHILLIPS EMERSON, A. B., M. D.,

Resident Physician, The Johns Hopkins Hospital; Associate in Medicine, The Johns Hopkins University.

During the past few years we have collected a series of records of blood examinations which are, we believe, the equal in accuracy of any yet published, and therefore of interest to report. We refer to the blood examinations made by our students of their own or of their classmates' blood during the course in clinical microscopy and clinical chemistry. This course is a part of the third year curriculum. Considerable work is done outside of class hours, and this includes practice with various blood instruments until they have become familiar and have attained a high degree of accuracy with their use.

It may seem, after reading this article, as if we allowed this practice with blood instruments to take too much time, and demanded an accuracy which was unnecessarily exact for clinical use. We know that during their fourth year as clinical clerks our students will not take half the time for a blood examination that they do during their third year, and that any method to be of clinical value must be brief. But only he can do quick work of even approximate accuracy who has previously done slow accurate work with this or a similar method. Hence, during their third year our students practice on themselves and on each other, handing in reports of the work done. Many students of the past five years attained a high degree of accuracy and experimented further, making many observations of considerable value. It is on these studies that this paper is based.

RED BLOOD CELLS.—The statement is commonly made that the red-blood-cell count of a normal man is 5,000,000, and of a normal woman, 4,500,000 cells per cubic millimeter. One gets the idea that these are fairly fixed values with normally rather narrow limits of variations, much as is true of the temperature, and, hence, one is often surprised at the variations in blood counts.

Our students practice counting as follows: The blood is taken from the ear, the finger or the forearm, in the latter case an area without pain-point over a vein being selected. Great care is taken that the part chosen is not cyanotic from position or pressure. The Thoma-Zeiss apparatus is used, with Toisson's fluid as diluent, and in a dilution of 1 to 200. The students make with each mixture two counting chamber preparations and count on each four, usually the corner, units. A unit consists of twenty-five small squares, or one-sixteenth of a square millimeter. Hence, eight units or one-half a square millimeter are counted from two drops of the mixture. Twenty-five cells is the greatest difference allowed between any two of these eight units. Good mixing in the pipette insures that the two drops should agree closely, and careful spreading on the slide that the four corners of each should be nearly uniform. The student makes a preliminary series of counts to familiarize himself with the method, and then starts a series, counting on successive days at the same hour each day, until the difference between two successive days is not over 200,000 cells. At the same time the above mentioned agreement of units must be obtained. This latter requirement of units is the more exacting of the two, for if that is fulfilled on two successive days the two total counts will usually fall well within the 200,000 cell unit, and to require 100,000 cells as the maximum difference would not be a much more difficult task for the student, as a glance at the following table will show. In the records of the blood examinations of 172 students, men and women, there was stated just what the difference between the counts of the two successive days was.

TABLE I.

Difference between counts of two successive days.	Number of cases.
0 to 20,000 red cells	25
20,001 to 40,000 " "	26
40,001 to 60,000 " "	28
60,001 to 80,000 " "	33
80.001 to 100,000 " "	23
100,001 to 120,000 " "	12
120,001 to 140,000 " "	10
140,001 to 160,000 " "	5
160,001 to 180,000 " "	6
180,001 to 200,000 " "	4

Thus the differences in 135 or nearly 80 per cent of the cases were 100,000 or below, and the mean of all was 64,200 cells.

We wish to report the red cell counts made on 171 students, all young men, and all in good health. Their ages were as follows:

TABLE II.

20 and 22 years	2
23 and 24 "	50
25 and 26 "	62
27 and 28 "	37
29 and 30 "	8
31 and 32 "	3
33 and 35 "	2
Doubtful	7

In the case of 150 students the records are perfectly complete and hence there is no doubt but that the counts answered the specifications required above. These 150 constitute Group A, Table III. We have little doubt but that the records of the other 21 are as accurate as these, and report the whole 171 as Group B. To show how little influence age between the years 20 and 35 has over the count, we have grouped the

149 students between 23 and 28 years of age as Group C. The averages of the two counts on the successive days are here reported.

TABLE III.

Red cells per cubic millimeter.	Groups A		Groups B		Groups C	
4,500,000 to 4,700,000	1		1		1	
4,700,001 to 5,000,000	6		8		8	
5,000,001 to 5,200,000	22		22		18	
5,200,001 to 5,400,000	22		25		25	
5,400,001 to 5,600,000	31		35		30	
5,600,001 to 5,800,000	32	84%	38	83.5%	31	82.5%
5,800,001 to 6,000,000	19		22		19	
6,000,001 to 6,200,000	9		10		8	
6,200,001 to 6,400,000	3		4		4	
6,400,001 to 6,600,000	2		2		2	
6,600,001 to 6,800,000	3		3		3	

The physiological limits for the counts for normal young men, as judged by our students in this climate, and during the months of October to February, are 4,500,000 and 6,800,000. In the case of over 82 per cent of the cases examined the limits were 5,000,000 and 6,000,000, while for 45 per cent, or nearly one-half, the counts lay between 5,400,000 and 5,800,000. The mean count, that is, that figure around which most counts lie, and which is not influenced by the extremes, as is the average, was, for Group A, 5,440,000; Group B, 5,430,000, and Group C, 5,454,000. Our "average" student, therefore, has a count of about 5,440,000; yet it does not mean that the student with 4,500,000 red cells was necessarily anæmic, nor that he with 6,800,000 was necessarily polycythæmic. These counts were apparently normal for those men at that time.

The count if taken at the same hour each day over short periods of time is remarkably constant. The following are the counts of one student on eight consecutive days:

5,180,000	5,136,000
5,104,000	5,060,000
5,000,000	5,140,000
5,184,000	5,000,000

Over longer periods of time, however, the count may vary much. The statement is made that the variations between summer and winter are considerable. We have no counts to test this, since our work is all in the fall and winter, yet the following cases would indicate such variations.

L.	Oct.	26	5,212,000
		27	5,296,000
		28	5,160,000
	Dec.	8	5,524,000
		9	5,532,000
H.	Nov.	27	4,656,000
		28	4,556,000
	Dec.	20	4,812,000
		21	4,784,000
		22	4,832,000
P.	Dec.	3	5,764,000
		4	5,728,000
	Jan.	15	5,932,000
		16	5,928,000

And others show no such changes.

S.	Nov.	18	5,816,000
		19	5,772,000
		21	5,856,000
		22	5,824,000
	Jan.	10	5,620,000
		11	5,688,000
V. d. H.	Nov.	7	5,532,000
	Dec.	10	5,424,000
		11	5,485,000

HÆMOGLOBIN.—The estimation of hæmoglobin is theoretically more valuable than the red count, since it is much more quickly and easily done. Theoretically, also, it should be more accurate, but as a matter of fact it is the most inaccurate part of our blood examination, and it is the instruments which are to blame for this.

The experience of this clinic is as follows: Formerly one make of instrument (v. Fleishl) was used on all the wards. Every one was satisfied for the results were comparable, but they were not correct. Then four different kinds of instruments (Fleishl, Miescher, Gowers, Dare) were put in use, and the ward workers trained to be skilled in the use of all. The readings were often ridiculously different, evidence of the inaccuracy of the several instruments, and yet the results were salutary. The men learned the weak points in each instrument. Then the same makes were kept in use, but all standardized to one particular instrument, a Miescher. The results were at once better. Our tendency now is to return to one form of hæmoglobinometer. All the several instruments will be regulated with one accepted as the standard. We are now experimenting with the new Sahli hæmometer in hopes this will prove satisfactory. At present it is not, since the instruments read even 30 per cent too high, but that is a simple matter of restandardization.

The essential points in a satisfactory hæmoglobinometer are: simplicity, a one-color standard, convenience and speed in use, and a reduction in value of the personal equation. The maker may mark it as he will, (and he does it poorly), but it should not be difficult to restandardize it to a fresh solution of hæmoglobin. Instruments requiring fifteen to thirty minutes for a determination, or a dark room are almost prohibited; those with color prisms are too hard to standardize and hence to restandardize. The Tallqirst allows too much of the personal element to enter, and we look forward to an instrument taking only a little longer and allowing readings correct to within 2 to 5 per cent.

Whatever instrument is chosen it should be one reading "grams" and not "per cent." Weight is something which we can understand and verify; per cent means relation to normal, the latter expressed as 100. But how does this work out? In the first place, there is no hæmoglobin content which is normal for all ages. Normal for a child would be too low for an adult. To say that a child, using an instrument reading 100 for adults, has 80 per cent hæmoglobin suggests that the child is anæmic, whereas that figure expresses an amount which is normal (that is, 100 per cent) for the child. Again,

who is to say what is normal? It must be a certain weight of hæmoglobin per 100 ccs. of blood. But one instrument is standardized using the color of a 13.7 gms. per 100 ccm., another a 14 gms., and still another a 14.5 gms. solution, and one confessed to having used a 17 gms. solution to determine the 100 point. Evidently 100 per cent is a pretty variable point and we do not wonder that the same blood at the same time can on different instruments read both 90 and 120. Since the makers must (or claim to, although we often doubt they take the trouble) make up a hæmoglobin solution of known weight per cent, why can they not state this weight on their instruments? Why not mark the scales off in grams, leaving us to decide whether the reading of a given blood is normal, *i. e.*, 100 per cent, or not? Examination of our figures might lead one to question whether or not our instruments really varied so much. The reason ours agree as well as they do is that of the eight or more instruments of various makes bought each year, we have to send back sometimes one-half to be replaced by others better standardized. This a practitioner buying but one would hardly do.

And, lastly, we want an instrument in the use of which the personal equation is not the important factor. We can all guess percentages. We know men whose guesses from a drop of blood on a rag, and the Tallquist scale is only a refinement of this method, are fairly accurate. But an error of 10 to 15 per cent is too great to be satisfactory to most careful workers. No one would now allow a real cell count to be stated as "75 per cent of normal." We demand the count itself. So we should demand the actual amount of hæmoglobin, and the latter should be as accurate or more so than the former.

A study of our students' reports of their bloods, using these various instruments, is of interest.

	Dare	Fleishl	Gowers	Tallqirst
65 to 70	1	3	3	
70 to 75	1		2	
75 to 80	8	9	5	1
80 to 85	10	20	13	9
85 to 90	23	25	14	14
90 to 95	50	52	46	33
95 to 100	51	32	36	34
100 to 105	3	11	16	
105 to 110	4	5	7	
110 to 115		3	2	
115 to 120	1		2	

With the Dare instrument 152 bloods were examined. Of these 101 lay between 90 and 100 per cent, and the mean figure was 93 per cent.

With the Fleishl instrument 158 bloods were examined. These varied somewhat more than those with the Dare, 129 lying between 80 and 100 per cent, and the mean of all was 92 per cent.

With the Gowers instrument 146 bloods were studied. Of these 82 lay between 90 and 100 per cent, and the mean of all was 94 per cent.

With the Tallqirst scale 91 determinations were made, with a mean of 93 per cent. It might seem at first sight as if the narrow limits of these last figures indicated the accuracy of this method. We consider it quite the reverse, that subjectively the observers have raised the values to nearly 100 per cent the "normal value."

The Miescher modification of the Fleishl instrument is, we are sure, the most accurate of the instruments mentioned. This is not an instrument for ordinary clinical use since it takes too much time, a dark room, and too much practice. This is the best instrument by far to train the accuracy of the students in color work, since the results are so well controlled. Our students examine the same blood by this method on two successive days at the same hour each day. A difference of 0.2 gms. was allowed. We have 121 such records and use here the average of the two determinations.

11 to 11.9 gms	2 students.
12 to 12.9 gms	7 "
13 to 13.9 gms	16 "
14 to 14.9 gms	35 "
15 to 15.9 gms	30 "
16 to 16.9 gms	25 "
17 to 17.9 gms	6 "

The majority, 106 bloods, read between 13 and 17 gms. The mean was 15.13 gms. It will be noticed that by this method the variations are the greatest. One would expect this since the variations in the count are great, hence those in hæmoglobin are probably as great.

COLOR INDEX.—This most valuable figure is the quotient of the hæmoglobin per cent, the numerator, and the red-cell per cent (5,000,000 as 100 per cent) denominator. For a normal person this should be 1. But using the figures of our "average" student, it is with the Fleishl instrument 0.86, with the Dare, 0.88, and with the Gowers, 0.87, all of them being values which are usually considered distinctly "chlorotic." We believe the color index could be more correctly expressed in terms of the amount of hæmoglobin per one million cells. We asked some of our students to so arrange their work that a count and hæmoglobin estimation with the Miescher instrument could be made on the same blood at the same time. We have records of but 21 different bloods examined in this way with several determinations on each blood, but they are quite enough. We give here the average for each student.

Grams of Hb. per 1,000,000 cells.	Number of cases.
2.20 to 2.39 gms	4
2.40 to 2.59 gms	5
2.60 to 2.79 gms	8
2.80 to 2.99 gms	3
3.43 gms.	1

The mean of these is 2.68 gms., and the average is 2.63 gms. It is interesting that while the weight per corpuscle in different persons varies somewhat, the values found in the same person at different times vary but little, even though the absolute values of cells and hæmoglobin vary considerably.

The following figures are the values in students found at fairly long intervals.

Sl.	3.43	3.45	3.41
H.	2.80	2.83	
P.	2.72	2.71	2.77
Wi.	2.66	2.69	
We.	2.39	2.38	
Ki.	2.90	2.96	

These are few of many illustrations. Accepting the figure 2.65 as the average weight per 1,000,000 cells we propose to use this as the denominator of a fraction, the numerator of which is the corresponding value for the case in question. For a practical illustration of this the reader is referred to the report by Mr. Wroth, who very kindly followed a few cases in this clinic. This paper will appear in a forthcoming number of the Bulletin.

Leucocytes.—The question of the leucocyte count of the normal person is a more difficult one to handle, since this varies within such wide limits. We required each student to make three counts: one with Toisson fluid, dilution 1:200; one with acetic acid (1 per cent), dilution 1:100; one with this same acetic acid, dilution 1:20. Counts on one blood at the same time by these three methods vary but little. We give the highest and the lowest counts in the case of 167 students.

Lowest counts:

2,000 to 4,000	2	students.
4,000 to 5,000	12	"
5,000 to 6,000	25	"
6,000 to 7,000	48	"
7,000 to 8,000	45	"
8,000 to 9,000	26	"
9,000 to 10,000	4	"
10,000 to 13,000	5	"

The mean count of this group is 7000.

Highest counts:

4,000 to 5,000	1	student.
5,000 to 6,000	9	students.
6,000 to 7,000	17	"
7,000 to 8,000	42	"
8,000 to 9,000	34	"
9,000 to 10,000	35	"
10,000 to 11,000	12	"
11,000 to 12,000	12	"
12,000 to 13,000	4	"
14,000	1	student.

The mean of these counts is 8400.

We, therefore, conclude that for our students the "average" leucocyte count is between 7000 and 8400.

Counts in Women.—We have records of the blood of but 16 women students examined in just the same manner as in the case of the men. The ages of these women varied from 22 to 32 years.

The red counts were:

4,300,000 to 4,500,000	3	students.
4,500,000 to 4,700,000	5	"
4,700,000 to 4,900,000	2	"
4,900,000 to 5,100,000	5	"
5,300,000 to 5,500,000	1	student.

The hæmoglobin estimations, the mean values given, were: Miescher, 11 gms.; Dare, 87 per cent; Gowers, 82 per cent, and Fleishl, 85 per cent. Their lowest leucocyte counts varied from 5000 to 13,000, the mean being 7100; the highest from 5000 to 16,000, the mean being 9500.

NOTES ON NEW BOOKS.

The Eye and Nervous System. Their Diagnostic Relations by Various Authors. Edited by Wm. Campbell Posey, A. B., M. D., Professor of Ophthalmology in the Philadelphia Polyclinic, Surgeon to the Wills Eye Hospital, etc., and William G. Spiller, M. D., Professor of Neuropathology and Associate Professor of Neurology in the University of Pennsylvania, etc. Illustrated. (*Philadelphia and London: J. B. Lippincott Company, 1906.*)

With the exception of Wilbrand and Sänger (Neurologie des Auges) nothing like the present volume has been presented to the profession within later years. The work of Wilbrand and Sänger is not the only one which has appeared on this subject in Germany, but in this particular field of medical literature it leads all others in completeness, not only in its own country but elsewhere. So far as we know "The Eye and Nervous System," by Posey and Spiller, is the only work of the kind in the English language. That it was needed seems reasonably certain and that it will meet with favor among a limited few is likely. It will be read by ophthalmologists and neurologists, especially by the latter, but it will not find its way certainly to any great extent into the library of the general practitioner. The volume contains not far from a thousand pages and consists of a series of monographs (twenty-four in all) by various authors. A work from the hands of several of the best ophthalmologists and neurologists in this country is apt to be of a high order and we regard it as such. The aim of the editors has been to present ophthalmo-neurology in such a manner that the general practitioner may without difficulty become conversant with its symptomatology; they have been aided in their efforts to do this by men who have distinguished themselves in these two branches of medicine. Although this aim is truly worthy we doubt the expediency of introducing so much material that is purely technical or scientific as opposed to that which is clinical or practical, for while the reader gains a more exhaustive treatise he becomes burdened with much that appeals neither to his understandings nor his sympathies.

We notice here and there careless spelling. Whatever simplification of spelling methods the future may have in store for those who dwell within the boundaries of these United States there is as yet no excuse for blundering over such names as Strümpell (page 649), Hirschberg (page 554), Shumway (page 536), and such a word for example as *sequelæ* (page 737).

These, however, are blemishes which do not materially mar the intrinsic worth of a work which contains a vast amount of valuable information and which testifies to the enterprising char-

acter of the School of Ophthalmology which has flourished so long and so honorably in Philadelphia.

Primer of Psychology and Mental Disease. By C. B. BURR, M. D. Third edition. (*Philadelphia: F. A. Davis Company, 1906.*)

It is always a pleasure to note the success that an author has with his book, and the call for a third edition of this primer is evidence that it has been helpful to those students to whom it is addressed. It is a most difficult task to condense into such small space the two broad subjects of psychology and insanity, but the author has presented them in a clear and succinct form, and one which makes easier for the student who desires to study further along these lines to understand the larger and profounder works which deal with these topics. Not having the first two editions at hand it is impossible for the reviewer to compare this last edition with the earlier ones, but this seems unnecessary in that the primer as it now appears is well adapted to its end. The only criticism to be made is in regard to the author's use of English, and if a fourth edition is called for, as it is to be hoped may be the case, it will be easy for him to make the necessary corrections, which are but few in number; such lapses as the use of "recoverable" for "curable," and "soluble" for "loose," are mere evidences of hasty writing and do not diminish the intrinsic value of the book. R. N.

History of the Boston City Hospital, 1864-1904. Edited by a Committee of the Hospital Staff. (*Boston: Municipal Printing Office, 1906.*)

A city hospital which for forty years has been managed so honestly and capably, with "politics" interfering and hampering its administration but little, deserves to have its history written, and it is a pleasure and interest to read this book. In it is to be found not only a full description of the hospital and its growth in size and production, but reminiscences of trustees, doctors, house officers, and nurses who have worked in the hospital; the most complete history of its sort perhaps on record. So many able and well-known physicians and surgeons have been connected with the City Hospital, and so much excellent work has been done within its walls, that these men deserve to have their work and name commemorated in this pleasant manner. The men and their work are the best proof that a city hospital, free from "politics," can produce as good work as a private hospital, and it is to be hoped that "politics" will never get the upper hand in this hospital. Not alone Boston, but Massachusetts and the other States may be proud of the City Hospital. R. N.

The Harvard Medical School, 1782-1906. (*Privately printed by the Medical Faculty, 1906.*)

As a fitting close to the interesting ceremonies at the dedication of the new buildings for the Harvard Medical School, the faculty of the school has issued this most handsome volume. The history is presented in a brief account of each department, arranged in chronological order, with a protrait of the first occupant of each chair—"provided he be not now alive,"—only one portrait is lacking in this series of noteworthy physicians, that of Dr. Aaron Dexter, the first Professor of Chemistry and Materia Medica. There are also illustrations of the different buildings which have housed the school since its commencement, 124 years ago, which mark, as perhaps nothing else would, the growth of medicine, as a science and profession, since the end of the eighteenth century. Such a history will be valueless a hundred years hence, and the faculty of the Harvard Medical School is to be most warmly congratulated on its publication.

R. N.

A Statement of Facts and Explanations on Leprosy and Fish-Eating. By JONATHAN HUTCHINSON, F. R. S., LL. D., formerly President of the Royal College of Surgeons. (*London: Archibald Constable & Co., Ld.; Chicago: W. T. Keener & Co., 1906.*)

This remarkable book, not only remarkable but extremely interesting, is the elaboration of a theory which the renowned author has upheld for fifty years. As he asserts in the preface it is not only written for medical men but also for the public, especially those who live in countries where leprosy occurs. The purpose of the book is to bring forward a mass of evidence which is both historical in character and also the result of wide and extensive personal observation in Europe, India, and South Africa, the effort being to demonstrate that leprosy is brought about chiefly by the eating of fish in a state of decomposition or badly cured.

The author shows further that leprosy is not contagious by touch, that segregation is and has always been totally insufficient to suppress the disease and has never caused it to decline. He also asserts that whenever there is plenty of salt in the curing of fish there is no leprosy.

As the result of careful investigation the author demonstrates that this disease is most prevalent in islands and along the shores of continents. In Norway where leprosy is and has always been for many generations prevalent the natives prefer to eat fish in a state of partial decomposition.

After the discovery of the bacillus of leprosy by Hansen, Hutchinson hoped this organism would be found in fish, but it has not yet been found in them; evidence however has been collected, according to the author, to prove the fish theory without demonstrating the presence of the bacilli in fish.

The author discusses all the theories about contagion and the occurrence of the disease in persons who have never eaten fish, and finds that most of the statements supporting the latter contention are not to be relied on and that the very large majority of the cases all the world over are most probably to be explained by his fish theory. The author has to explain some undoubted cases of leprosy in which it could not be proven that fish had ever been eaten; in these cases he thinks the disease was due to eating food which had been handled by lepers. He calls this the "indirect" or commensal method, which also explains why the disease is apt to cling to certain families and run in successive generations.

The attempt to isolate lepers always has been, he says, and always will be illusory.

The author practically discusses, in this work, the subject of leprosy in a most entertaining and lucid manner from every standpoint, its origin, its antiquity, its symptoms, its distribution, etc.

He declares leprosy is not necessarily fatal, but that it may be averted at any stage, and if all lepers were liberally fed and properly cared for few would probably die of this disease.

The author makes some rather startling statements, for example (page 31), that leprosy and tuberculosis are allied diseases, as both are well nigh ubiquitous, and are actively propagated by the use of special foods. He also suggests that the bacillus of leprosy and the tubercle bacillus may have a common ancestry. He does not believe in the theory that tuberculosis spreads by contagion, but thinks that the tubercle bacilli is ubiquitous and exists in us all and only awaits suitable conditions to develop.

On page 45 is a statement that tubercle bacilli may in some individuals become modified in some inexplicable manner, *e. g.*, by badly cured fish which may so affect the bacillus within the body that leprosy instead of tuberculosis is the result.

Elsewhere the author suggests that the leprosy bacilli may develop in fish under conditions of decomposition, although such a development may be very exceptional, yet it is always possible.

Hutchinson believes that the disappearance in some places and the marked decrease in others of leprosy during the Middle Ages was due to the spread of Protestantism, which did away with the compulsory eating of fish two days a week.

The author asserts again and again that the disease is not contagious and cites a mass of evidence of various kinds to prove this statement; *e. g.*, there are many scattered lepers living in London, Paris, Vienna, Berlin, and in the United States, yet one never hears of any contagion nor of any epidemic. Cases have been frequently recorded where a husband having leprosy and a wife free of it have lived together for many years without the latter contracting the disease.

In a Madras (India) asylum there were 148 couples where the husband was a leper but the wife not; and in 43 other couples the conditions were reversed, the wife was a leper and the husband not; but all these couples lived together as if both husbands and wives were in good health. Attendants in leper asylums seldom contract the disease.

For many years numbers of lepers, as the author states, emigrated from Norway to the United States, yet no one maintains that the disease has spread in the United States. Hutchinson's thorough investigation of the evidence at hand seems to show that leprosy is not contagious.

In a discussion before a medical society in Cape Colony to a local doctor who said he would never accept the fish theory until the bacillus had been demonstrated as being present in fish, Hutchinson answered, "a blessing was promised to those who could on occasions believe without having seen."

It is rather curious to note that all attempts at inoculation have failed up to the present.

As the result of his "fish theory" the author compares leprosy to chronic ptomaine poisoning.

To sum up, Hutchinson has collected a remarkable amount of direct and indirect evidence which almost convinces the reader that leprosy is due to eating bad fish, although the bacillus of leprosy has never been demonstrated in them. The advice which he therefore urges strongly is, do not eat bad fish or badly-cured fish or you may contract leprosy. This may sound rather ridiculous to the people of the United States, England, Germany, etc., but is very necessary for those who live where leprosy abounds.

Now what are the opposing views to the fish theory? They are: 1. All cases of leprosy cannot be explained in this way. 2. The bacillus of leprosy is found in practically all cases of this disease and yet has never been demonstrated in fish. 3. Recent investigations, by Dr. Goodhue of Hawaii, have shown that bed bugs may be the carriers of the disease, as the bacilli have been found in them and also in mosquitoes; but Dr. Arning, when in the Sandwich Islands, examined mosquitoes after they had bitten the cutaneous lesions of lepers and failed to find the bacilli in them.

When one looks back only a few years and remembers the many divergent views put forward about the cause and transmission of malaria as due to miasmas, telluric influences, etc., and compares them with the present scientific view one cannot but feel that the insect (bed-bug) theory of the transmission of leprosy is more likely to be proved correct than the fish theory.

The book can be highly recommended to those who are at all interested in leprosy.

The Journal of Hygiene. Vol. VI. No. 4. (*Cambridge, England: University Press.*)

This "extra" number of the above-named journal, containing "Reports on Plague Investigations in India," contains ten most valuable and interesting papers, illustrated with a number of plates, by the members of the committee appointed to pursue these studies; the articles consider various questions in relation to plague, as for instance, the transmission of plague by fleas, the species of fleas found upon rats, and the anatomy of the mouth parts and alimentary canal of the Indian rat-flea. There are other reports on the immunity of rats, on the infectivity by floors contaminated by the plague bacillus, on the existence of chronic plague in rats, etc. As is usual in the reports issued by English Government committees the work has been admirably done; the articles, though brief, are clear, well written, and important contributions to the subject of plague, and the complete, for this is but a preliminary report, will be awaited with eagerness. The necessity of such investigations is clear to all; plague is the most dreaded of all diseases in countries where it does not naturally exist, and the means taken by States to prevent its spread at moments when it is feared that even a single case may have entered a town are so expensive and burdensome to all the inhabitants that it is to be hoped that the results of the investigations now being pursued so carefully and thoroughly will help to aid all governments as to the proper methods to be used in guarding against a possible epidemic. R. N.

Conferences on the Moral Philosophy of Medicine. Prepared by an American Physician. (*New York: Rebman Company, 1906.*)

This small volume is entitled on its cloth cover "A Book for Medical Students and Young Practitioners;" but neither title gives a clear idea of its contents. The conferences are intended to serve as a guide to moral conduct for young doctors in all their relations with their patients, "confrères," and the public. Much of the advice given is good, but the work is a pretentious one, and the author has done well not to sign his name to it. It will do no one harm to read it, but it is doubtful how much benefit any reader will derive from it. There are other far better works on this subject. Although the author devotes a couple of chapters to doctors as writers, yet his own style is so bad oftentimes that his example is to be carefully avoided. His sentences are frequently too long, involved, and wrongly punctuated; and he has a bad habit of using too many adjectives. But perhaps his worst fault is in the use of rare words, or new words coined by himself. The following words used by him are not to be found in the Century Dictionary: Physiophist, logophylist (a favorite word of the author's), monstrate, etical, morphism, morphicly, etc. In the case of the last three words he advocates their use, respectively, for eitological, morphology, and morphologically. He says "pathic" or "morbid" should be used rather than pathological; his reason for this is not clear, nor does he explain the difference which he says exists between "autopsy" and "post-mortem examination," nor between "catheterization" and "catheterism," words which, according to the Century Dictionary, are interchangeable. Instead of pathology he says "patho-anatomy," which is certainly a poor substitute. He uses "olfactive" for "olfactory," and "sensual" for "sensuous"—both serious errors; again, "ungrammatic" for "ungrammatical." He speaks of "verbal bankruptcy"—a condition from which he seems to suffer, when he uses the word "macrology." One quotation to close with, and all will have been said that is necessary to convict the author of an uncultured style: "The prudent young scholar will tactfully avoid verbal encounters with the vulgar and never unsheath his intellectual weapons against those gigantic word-mills that perpetually grind out all manner of literary heresies." R. N.

NOTES AND NEWS.

Dr. John Auer is Fellow of the Rockefeller Institute and Instructor in Physiology, Harvard Medical School. Address: 107 West 122d Street. New York.

Dr. J. M. Berry is Orthopedist to the Samaritan Hospital, Troy, N. Y. Address: 75 Fourth Street, Troy, N. Y.

Dr. George Blumer is Professor of Theory and Practice of Medicine in the Yale Medical School.

Dr. Walter V. Brem is Physician at the Ancon Hospital, Ancon, Canal Zone.

Dr. Thomas R. Brown is Associate in Medicine, Johns Hopkins University; Assistant Physician, Johns Hopkins Hospital Dispensary; Associate Editor, Maryland Medical Journal; Attending Physician, Union Protestant Infirmary; Consulting Physician, Frederick City Hospital.

Dr. H. W. Buckler is Assistant in Obstetrics, Johns Hopkins University; Professor of Medicine and Therapeutics, Woman's Medical College; Clinical Assistant in Medicine, Johns Hopkins Hospital Dispensary; Consulting Physician, Maryland Hospital for Consumptives; Director, Maryland State Tuberculosis Sanitarium; Medical Superintendent, H. A. Kelly Sanitarium.

Dr. C. H. Bunting is Professor of Pathology, University of Virginia, and Pathologist to the University Hospital.

Dr. Camillus Bush is Instructor of Surgery in the University of California and Visiting Surgeon to the St. Helena Sanitarium. Address: 2200 Steiner Street, San Francisco.

Dr. C. B. Camac is Visiting Physician to the City Hospital, New York City; Head of the Medical Sub-Department of Physicial Diagnosis Instruction and Lecturer in Medicine, Cornell University Medical School, New York.

Dr. E. D. Clark is on the Staff of the City, St. Vincent's and Deaconess Hospitals and City Dispensary, and is President of the City Board of Health, Indianapolis.

Dr. Thomas Wood Clark is Acting Clinical Assistant at the Hospitals for Sick Children, Great Ormond Street, London. His address is 5 Torrington Square, London, W. C.

Dr. John W. Churchman is Acting Second Assistant Resident Surgeon, Johns Hopkins Hospital.

Dr. John Staige Davis is Clinical Assistant, Surgical Out-patient Department, Johns Hopkins Hospital; Surgeon to Out-patient Department, Robert Garrett Children's Hospital; Assistant Demonstrator of Anatomy, College of Physicians and Surgeons, Baltimore.

Dr. Geo. W. Dobbin is Professor of Gynecology and Obstetrics, College of Physicians and Surgeons; Obstetrician in Chief to the Maryland Lying-in Asylum; Consulting Obstetrician to the Baltimore City Hospital and the Bay View Hospital.

Dr. Joseph Erlanger is Professor of Physiology, the University of Wisconsin.

Dr. W. W. Farr's address is 117 Allen's Lane, Mt. Airy, Philadelphia.

Dr. A. B. Herrick is Chief of the Surgical Clinic at the Ancon Hospital, Canal Zone.

Dr. Gerry R. Holden is Associate Gynecologist to St. Luke's Hospital, Jacksonville, Fla.

Dr. Campbell P. Howard's address is the Montreal General Hospital, Montreal, Canada.

Dr. Frank W. Lynch is Assistant Professor Obstetrics and Gynecology, Rush Medical Colege, and Assistant Visiting Obstetrician and Gynecologist, Presbyterian Hospital, Chicago.

Dr. James D. Madison is Professor of Medicine, Wisconsin College of Physicians and Surgeons; Attending Physician at the Milwaukee County Hospital, St. Joseph's Hospital and Johnson's Emergency Hospital.

Dr. E. W. Meisenhelder, Jr., is a member of the Gynecological Staff, York City Hospital, and Lecturer in Obstetrics and Gynecology to the Nurses Training School, York City Hospital.

Dr. John I. Middleton is Assistant Surgeon to the Opthalmic Department of the New York Eye and Ear Infirmary and of the Randall's Island Hospital.

Dr. James F. Mitchell is Assistant Professor of Surgical Pathology in the George Washington University and Surgeon to the Providence Hospital.

Dr. W. Bean Moulton is Adjunct Surgeon to the Maine General Hospital; Assistant Surgeon, St. Barnabas Hospital and Instructor in Gynecology, the Medical School of Maine. His address is 622 Congress Street, Portland, Me.

Dr. Rupert Norton is Acting Superintendent of the Johns Hopkins Hospital during the year's leave of absence of Dr. Henry M. Hurd.

Dr. Geo. H. F. Nuttall was elected Reader in Hygiene at Cambridge and has since been appointed to the Quick Professorship of Biology in the same University. His address is 3, Cranmer Road, Cambridge, England.

Dr. Mary S. Packard is Physician, North End Dispensary for Women and Chidren, and Physician, the Children's Clinic of the Out-patient Department of the Rhode Island Hospital. Address: 425 Angell Street, Providence, R. I.

Dr. Theodore F. Riggs is Resident Surgeon at the Union Protestant Infirmary, Baltimore.

Dr. John A. Sampson is Clinical Professor of Gynecology in the Albany Medical College and Gynecologist to the Albany Hospital and the South-End Dispensary.

Dr. Benjamin R. Schenck is Secretary of the Michigan State Medical Society and Editor of the Journal of the Michigan State Medical Society.

Dr. Robert B. Slocum is Superintendent of the James Walker Memorial Hospital, Wilmington, N. C.

Dr. John A. Sperry is Second Assistant Resident Physician at the Union Protestant Infirmary, Baltimore.

Dr. Martin B. Tinker's address is Cornell University Medical College, Ithaca, N. Y.

Dr. Douglas Vanderhoof is Instructor and Clinical Assistant in Medicine at the Medical College of Virginia, Richmond.

Dr. Louis M. Warfield is Lecturer in Clinical Microscopy, Medical Department Washington University; Assistant Dispensary Physician, St. Louis City Dispensary; Attending Physician, Martha Parsons Hospital for Children. Address: 3806 Washington Avenue, St. Louis.

Dr. Sarah D. Wyckoff is Lecturer in Domestic Science and Hygiene in the High School at Wilkesbarre, and Gymnasium Examiner at the Wyoming Seminary, Wilkesbarre, Pa.

TO THE MEDICAL PROFESSION OF MARYLAND:

The medical profession of San Francisco lost its medical library, the San Francisco County Medical Society Library, in the fire last spring. Most of the physicians also lost whatever private libraries they had succeeded in collecting. A committee (named below) has been appointed by the American Medical Association and by the Association of American Physicians to collect and send books to San Francisco, both for the library and for private individuals when duplicate copies are sent on, as they are sure to be.

Will you send to Dr. W. S. Thayer, 406 Cathedral Street, Baltimore, Maryland, any medical books of value or bound volumes of journals which you can spare? Fairly recent editions of standard text-books, foreign text-books or bound journals (French, German, and Italian), hospital reports, monographs of all sorts, books on special subjects, old classics, (e. g. Trousseau, Charcot) and the Sydenham Society publications are especially desired.

Acknowledgment of all that is received will be made through the medical journals and the books will be packed and shipped as promptly as possible. Signed,

CHARLES L. DANA, Chairman, New York City.
R. C. CABOT, Secretary, Boston.

Frank Billings, Chicago.
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